

Bench-Stable Electrophilic Indole and Pyrrole Reagents: Serendipitous Discovery and Use in C-H Functionalization

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The development of reagents allowing the reversal of the standard reactivity (Umpolung) of small building blocks is an important field of research in chemistry, as it allows increasing the flexibility of organic synthesis. Indoles and pyrroles are ubiquitous heterocycles in natural products and drugs. They are usually functionalized making use of their high nucleophilicity. In contrast, only few methods are based on the use of electrophilic indole and pyrrole synthons, as the needed reagents are highly unstable or can be used only with a very narrow scope. Herein, we report the serendipitous discovery and first use in the C-H functionalization of arenes of IndoleBX and PyrroleBX, new thermally highly stable benziodoxol(on)e hypervalent iodine reagents. IndoleBX and PyrroleBX could be obtained in one step from the corresponding heterocycles and acetoxy benziodoxolone using a Lewis acid catalyst. The mild reactions conditions allowed the introduction of a broad range of functional groups, including ethers, halogens and boronic esters. The new reagents could then be used in the rhodium- and ruthenium- catalyzed C-H heteroarylation of arene rings bearing heterocyclic or benzamide directing groups. Such transformations could not be realized using previously reported C-H functionalization procedures.

Keywords: Heterocycles • Umpolung • Hypervalent Iodine • Indole • C-H activation

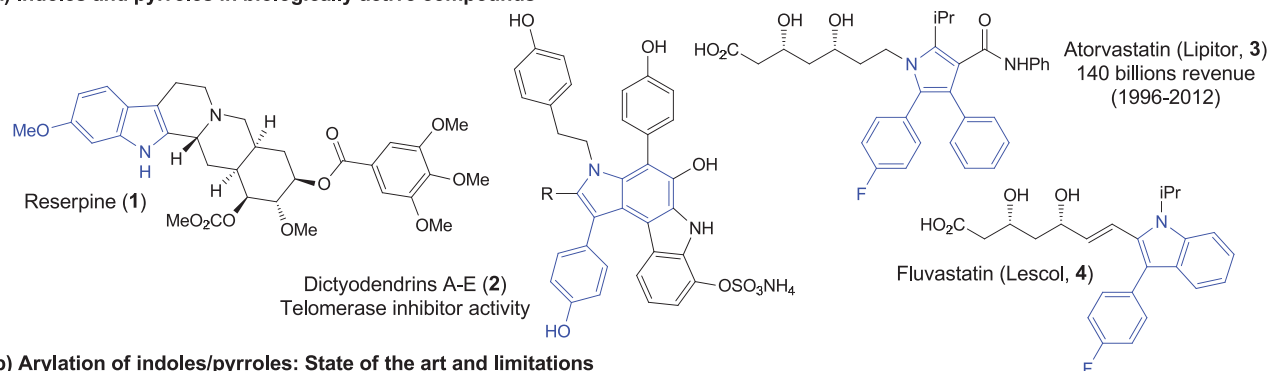
Introduction

Pyrroles and indoles are among the most ubiquitous azoles present in nature. These heterocycles can be found in pharmaceuticals,^[1] fragrances, agrochemicals and natural products (scheme 1a).^[2] First discovered in the late 19th century by Bayer,^[3] their popularity increased when many indole-containing alkaloids such as Reserpine (**1**)^[4] or Dictyodendrins A-E (**2**)^[5,6] were found to be biologically active. Indole and pyrrole rings are also well represented in top selling drugs such as Atorvastatin (**3**) and Fluvastatin (**4**).^[7] As a consequence of this interest, countless methods for both synthesis and functionalization of indoles and pyrroles were developed.^[8–10] As they are electron-rich heterocycles, they undergo electrophilic aromatic substitutions at a higher rate than the benzene ring.^[11] Of particular interest are arylation methods, as arylated heterocycles have found widespread applications in synthetic and medicinal chemistry. The most often used approach is cross-coupling, but it requires pre-functionalized building blocks and generates a significant amount of waste.

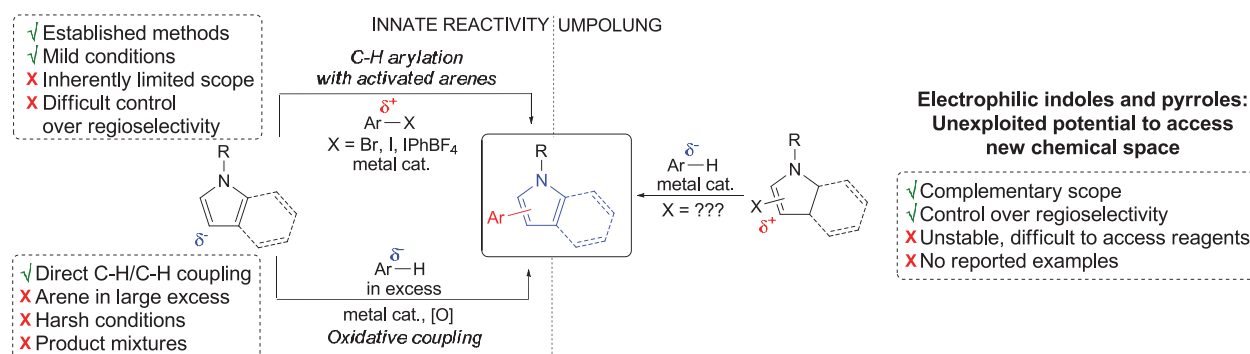
Recently, strong interest arouses in direct C-H arylation, as a more direct method for heterocyclic functionalization (scheme 1b). Most works have made use of the high nucleophilicity of indoles and pyrroles for C-H functionalization with activated electrophilic arene partners, such as halides.^[12] Of particular importance are the works of Sanford,^[13] Gaunt,^[14] and coworkers, in which electron-rich indoles and pyrroles are coupled with hypervalent iodonium salts in the presence of catalytic amounts of Pd(II) or Cu(I) under mild reaction conditions. Ackermann and coworkers also reported a metal free arylation of indoles with aryl iodonium salts.^[15] These works among others fully establish aryl iodonium salts as exceptional reagents for C-H functionalization under mild conditions.^[16]

However, the nearly exclusive focus on the innate nucleophilicity of indoles and pyrroles to couple them with electrophilic pre-activated arenes fundamentally limits the diversity of accessible structures. In this respect, Fagnou and co-workers reported the elegant direct oxidative coupling of two C-H bonds between arenes and indoles, which allows also the use of electron-rich partners (scheme 1b).^[17,18] However, this approach required a large excess of the arene and high temperatures, often resulting in regioisomeric mixtures of products and low functional group tolerance. More efficient processes were possible only in special cases, such as coupling with activated azoles^[19–24] or perfluorinated benzene rings.^[25,26] Therefore, the availability of *electrophilic* indole or pyrrole synthons able to react with *nucleophilic* arene partners by C-H functionalization would tremendously enhance the range of accessible arylated heterocycles. Nevertheless, accessing such synthons constitutes a formidable challenge. Only few successful approaches with a narrow scope of electronically biased substrates or relying on reactive electrophilic indolyl intermediates generated *in situ* have been reported.^[27] Hypervalent iodine reagents have been frequently applied to achieve the Umpolung of different nucleophiles.^[28–32] In particular, the Umpolung of indoles and pyrroles was realized by Kita and co-workers by *in situ* generation of non-isolable hypervalent iodine intermediates from phenyliodonium ditrifluoroacetate (PIDA).^[33] This approach was used in the total synthesis of indole alkaloids.^[34] These reports showed the possibility of nucleophilic functionalization of electron-rich heterocycles, via *in-situ* formation of hypervalent iodine intermediates. Nevertheless, the instability of the formed intermediates limited the scope and applications of these methods. Unfortunately, only few examples of isolable indole and pyrrole-based iodonium salts have been reported.

a) Indoles and pyrroles in biologically active compounds



b) Arylation of indoles/pyrroles: State of the art and limitations



Scheme 1. a) Examples of indole- and pyrrole-containing natural products and top selling drugs. b) State of the Art of transition metal catalyzed indole C-H arylation.

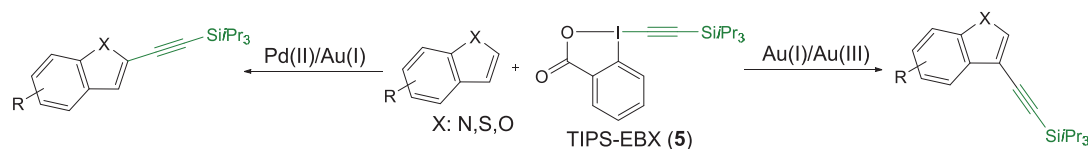
Indole-based iodonium salts were first reported in the 70s by Neiland and coworkers,^[35,36] followed by the groups of Kost,^[37,38] and Moriarty.^[39] A multi-step procedure *via* a spontaneously self-detonating betaine intermediate was required to access these reagents: the obtained salts were unstable and could again be used only for a limited range of transformations. Only halogenation^[37,38] and alkylation^[39] with organolithium reagents were reported. Recently, more stable azole-based iodonium reagents were reported by Suna and coworkers.^[40,41] Nevertheless, the azoles needed to be deactivated by electron-withdrawing groups in order to stabilize the reagents. Suna and coworkers reported two applications of these reagents: a Cu(I)-catalyzed azidation in which the final product was converted in situ *via* click chemistry,^[40] and an amination.^[41] More stable iodonium salts were reported by Moriyama,^[42,43] Kita^[44] and coworkers, but again, an electron-withdrawing group on the nitrogen was required to stabilize the reagents. Furthermore, a recent example of de-aromatization of indoles by using Neiland's *NH*-indole iodonium salt was reported by Liu *et al.*^[45] This still constitutes the only example of metal catalysis involving indole-based iodonium salts not stabilized by electron-withdrawing protecting groups. To the best of our knowledge, indole and pyrrole iodonium salts have never been used in the metal-catalyzed arylation of C-H bonds, probably because of their limited stability, especially at higher temperatures. Clearly, the development of better indole and pyrrole electrophilic synthons combining high reactivity with enhanced stability is urgently needed.

Since several years, our group has investigated the reactivity of more stable cyclic hypervalent iodine reagents in group transfer reactions.^[32] In particular, EthynylBenziodoXol(on)es (EBX) reagents have been used successfully for the Umpolung of alkynes.^[46,47] They were especially employed by us and others in metal-catalyzed C-H alkynylation of (hetero)arenes (scheme 2a).^[48–59] Recently, we have reported preliminary results on the synthesis and use of new stable indole- and pyrrole-benziodoxol(on)e reagents (Indole- and Pyrrole- BX) and their use in the Rh(III)- and Ru(II)-catalyzed C-H functionalizations of arenes.^[60] Herein, we present a full account of this work, including: (1) the serendipitous discovery of the reagents when attempting the development of further domino transformations for the synthesis of functionalized indoles based on our previous work in this area^[61–64] (scheme 2b), (2) a detailed report on the synthesis and structure analysis of both benziodoxole and benziodoxolone heterocyclic reagents and (3) details on the optimization and scope of the new C-H functionalization reactions (scheme 2c).

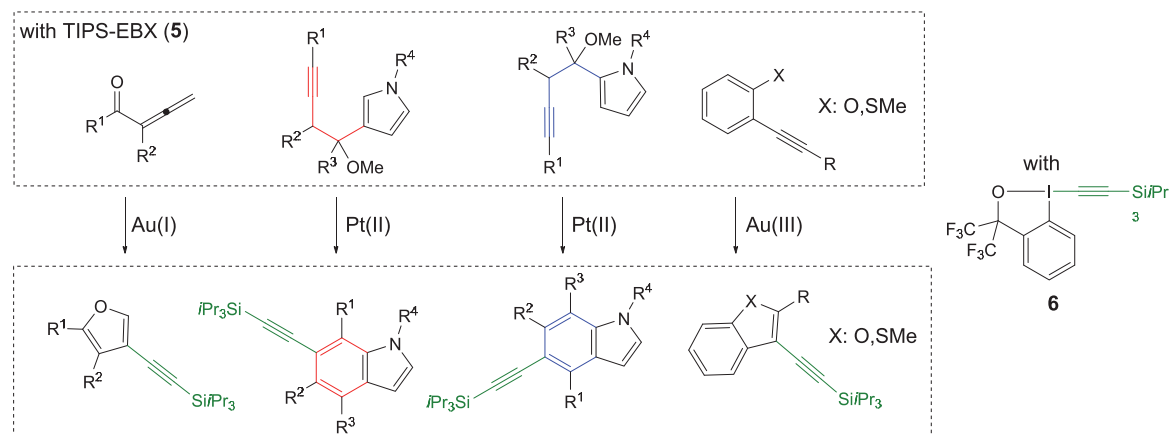
Results and Discussion

While direct functionalization methods of heterocyclic rings are well developed, they remain limited to more reactive C-H bonds, in particular the C2 or C3 positions in heteroarenes (scheme 2a). Metal catalyzed domino reactions constitute in this case an interesting alternative, as they give access to heterocycles functionalized at other positions. Our group reported several domino

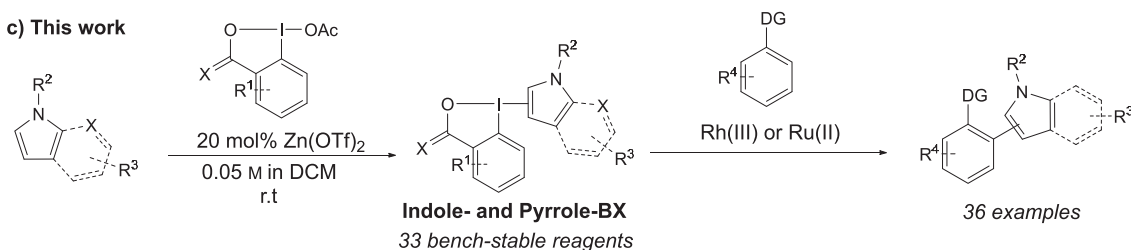
a) Selective direct functionalizations of heterocycles developed by our group



b) Domino reactions developed by our group



c) This work

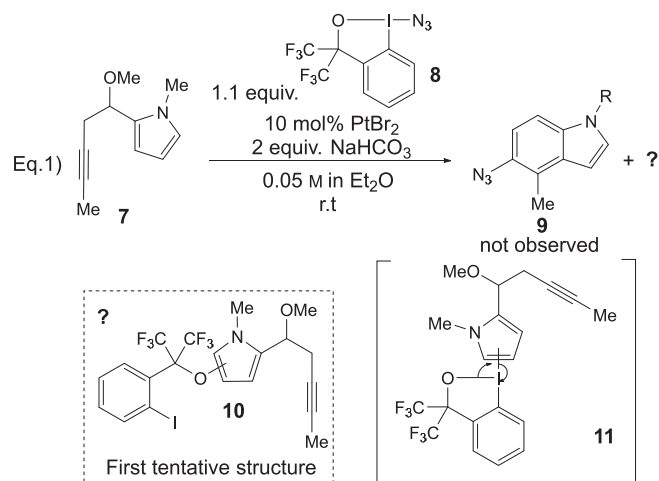


Scheme 2. a) and b) Previous work of the group on the synthesis of alkynylated heterocycles via C-H functionalization or domino processes. c) This work.

approaches for the synthesis of heterocycles alkynylated on the benzene ring (scheme 2b). C3-alkynylated furans were obtained starting from α -allenyl ketones.^[62] A gold(III) catalyst was initially used for this transformation, but in situ formation of an active gold(I) catalyst was proposed later based on computational studies.^[65] C5- and C6- alkynylated indoles were built starting from alkylated pyrrole precursors: Starting from C3-alkylated pyrroles C6-alkynylated indoles were obtained, while C2-alkylated pyrroles afforded C5-alkynylated indoles.^[63] Finally, several C3 alkynylated benzothiophenes and benzofurans were synthesized from aryl-thiols and phenols.^[64]

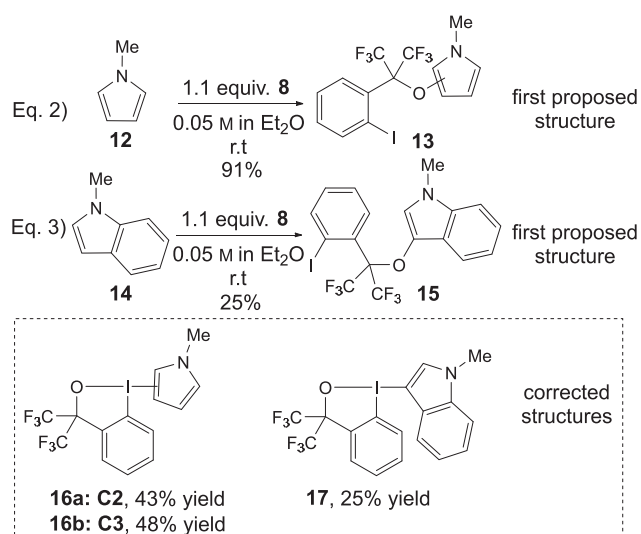
Based on these results, our initial aim was to expand the scope of domino transformations to other hypervalent iodine reagents, in particular azidobenziodoxol(on)es (ABX).^[66–68] Our choice of ABX was justified by the large number of applications and chemical modifications related to azides, such as reduction to amines or cycloaddition with alkynes^[69] and the recent success reported with this reagent for azide transfer reactions.^[70–78] Best results in the domino cyclization-alkynylation reactions had been obtained with hexafluoroisopropanol derived reagent **6**. Therefore the corresponding reagent **8** containing an azide was synthesized^[66] and the domino cyclization-azidation of pyrrole **7** was attempted under the conditions successful for alkynylation (the solvent was changed to solubilize the ABX reagent **8**). However, we did not obtain the desired

azidated indole **9**, but we observed the full conversion to a polar compound containing ¹H NMR signals corresponding to a 2-iodobenzoate ring and a substituted pyrrole, without modification of the alkyl substituent (Eq. 1). The same result was obtained in absence of the platinum catalyst.

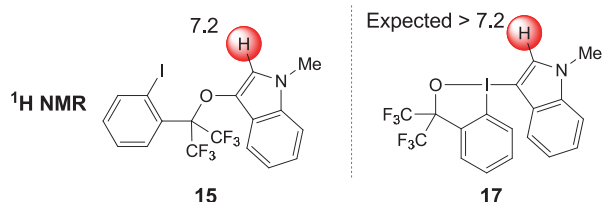


To explain the observed NMR spectra, we first hypothesized that a new C-O bond had been formed between the alcoholate and the pyrrole ring to give heterocycle **10**. Due to the good leaving group ability of the azide, nucleophilic attack of the pyrrole ring followed by re-aromatization and

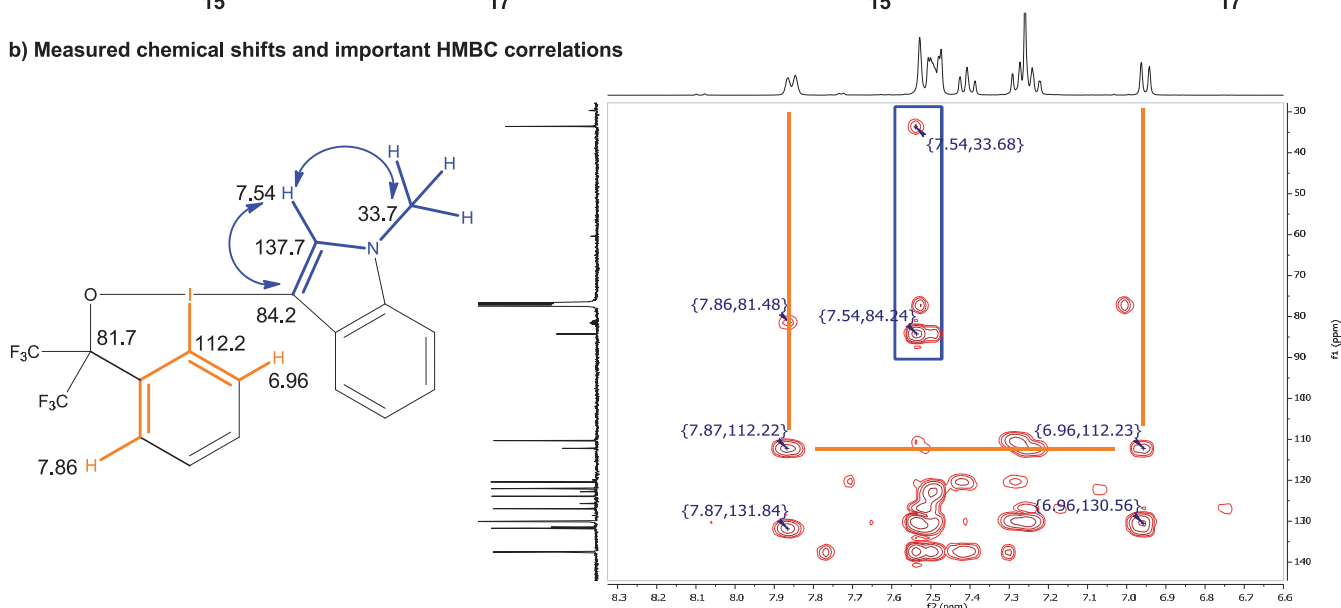
release of hydrazoic acid would give hypervalent iodine reagent **11**. At this stage, we speculated that this intermediate would be unstable and undergo reductive elimination to give **10**. Unfortunately, the new compound was unstable, and it was not possible to confirm its structure. As the new transformation did not involve the alkyne triple bond, we decided to study simple commercially available *N*-methyl pyrrole (**12**) and *N*-methyl indole (**14**) as starting materials (Eq. 2 and 3)). For pyrrole **12**, we again observed the formation of a 1:1 C2:C3-functionalized separable mixture of two highly polar regioisomers; these two compounds were stable and obtained in a combined excellent yield of 91% (Eq. 2). In case of indole **14**, a single C3-functionalized product was obtained in 25% yield (Eq. 3).



a) Expected ^1H and ^{13}C NMR shifts for proposed structures



b) Measured chemical shifts and important HMBC correlations



At this point, we still hypothesized that we had formed a new C-O bond with the heterocycle (structures **13** and **15**). However, extensive NMR analysis performed on the product obtained from indole **14** were not in agreement with this assignment, and fitted better with structure **17** still containing a hypervalent iodine atom (figure 1). First, the expected proton and carbon chemical shifts around the iodine atom were estimated for both envisaged structure **15** and **17** based on the reported values for 1-(1,1,1,3,3,3-hexafluoro-2-methoxypropan-2-yl)-2-iodobenzene,^[79] indoles bearing an oxygen substituent on the C3 position,^[80,81] hexafluoroisopropanol derived hypervalent iodine reagents^[62] and indole iodonium salts.^[26] The observed indole C2 ^1H signal at 7.51 ppm is in lower field than expected for a compound such as **15**, but this fact alone was not sufficient to support the hypervalent structure. Hypervalent iodine compounds can usually be easily differentiated from the corresponding iodines via the ^{13}C chemical shift of the adjacent carbon, which appears in about 20-30 ppm in lower field. However, in the specific case of the alternative structures **15** and **17**, the influence of the iodine atom and the indole core on the chemical shift are expected to compensate each other, leading in each case to two signals around 80-90 ppm and one signal at 110-120 ppm for the carbon atoms in proximity to the iodine atom (figure 1a). The observed values of 81.7, 84.5 and 112.2 ppm are in better agreement with the hypervalent iodine structure, but the difference is not enough to be sure of the assignment. Fortunately, the positions of the aromatic signals in higher field is different for the two proposed structures: on the benzene ring for **15** and on the indole for **17**.

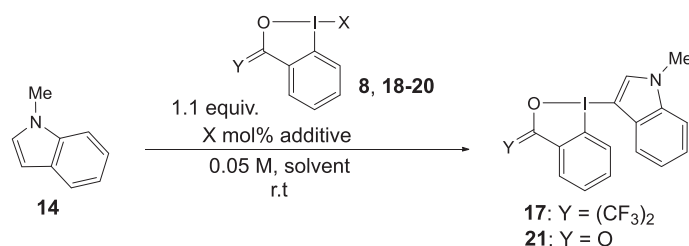
Figure 1. Structure assignment of **17** based on NMR analysis. All values are chemical shifts in ppm.

Extensive 2-D NMR experiments allowed a full assignment of the signals^[82] and unambiguously showed that the signal at 112.2 ppm was on the benzene ring and the one at 84.5 ppm on the indole, supporting hypervalent structure **17**. HMBC correlations between the arene C-H signals at 6.96 and 7.86 ppm and the quaternary carbon at 112.2 ppm, as well as between the C2 indole C-H signal at 7.54 ppm and the quaternary C3 carbon at 84.2 ppm were especially important for the structure assignment (Figure 1b).

Establishing the hypervalent structure of the obtained products was an important step, as benziodoxole-based indole or pyrrole reagents had never been reported before. We therefore decided to further improve the synthesis of these new "Indole-BX" and "Pyrrole-BX" reagents in order to study their properties and potential synthetic applications (table 1). Indole reagent **17** could be obtained only in 25% yield using azidobenziodoxole reagent **8**, (table 1, entry 1). The influence of the leaving group on the

iodine was first investigated. In fact, azido-substituted hypervalent iodine reagents are often unstable and toxic azide salts are generated during the reaction. We then decided to employ 1-acetoxy-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (**18**), a more stable and readily available reagent.^[83] However, no reaction was observed (table 1, entry 2). Lewis acids, in particular zinc(II) triflate, have been used by our group and others for the activation of benziodoxole reagents.^[71,84] In fact, when a catalytic amount of zinc(II) triflate was added, a promising 56% yield of **17** was obtained (table 1, entry 3). As hexafluoroisopropanol-derived hypervalent iodine reagents are expensive, we then tested 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (**19**)^[85] under these conditions, but the desired product **21** was not obtained (table 3, entry 4). In contrast, 36% yield of **21** was isolated starting from acetoxy benziodoxolone **20**^[86] (table 1, entry 5). No product was obtained in absence of zinc(II) triflate (table 1, entry 6).

Table 1. Optimization of the synthesis of IndoleBX **17** and **21**.



Entry	Reagent	Y	X	Solvent (m)	Additive (mol%)	Yield % ^a
1	8	(CF ₃) ₂	N ₃	Et ₂ O (0.05)	-	25%
2	18	(CF ₃) ₂	OAc	Et ₂ O (0.05)		- ^b
3	18	(CF ₃) ₂	OAc	Et ₂ O (0.05)	Zn(OTf) ₂ (10)	56%
4	19	O	OH	Et ₂ O (0.05)	Zn(OTf) ₂ (10)	- ^b
5	20	O	OAc	Et ₂ O (0.05)	Zn(OTf) ₂ (10)	36%
6	20	O	OAc	Et ₂ O (0.05)	-	- ^b
7	20	O	OAc	Et ₂ O (0.05)	TMSOTf (10)	16%
8	20	O	OAc	Et ₂ O (0.05)	Cu(OTf) ₂ (10)	36% ^c
9	20	O	OAc	Et ₂ O (0.05)	AgNTf ₂ (20)	- ^c
10	20	O	OAc	Et ₂ O (0.05)	TBAF (20)	- ^c
11	20	O	OAc	Et ₂ O (0.05)	AgF (20)	- ^c
12	20	O	OAc	THF (0.05)	Zn(OTf) ₂ (10)	
13	20	O	OAc	DCM (0.05)	Zn(OTf) ₂ (10)	full ^d
14	20	O	OAc	DCM (0.05)	Zn(OTf) ₂ (20)	97%

a) Substrate **14** (0.100 mmol), reagents **8**, **18-20** (0.110 mmol), additive (10-20 mol%), and solvent (0.05 M) at 25 °C. Isolated yield after flash chromatography is given. b) No conversion: starting materials recovered. c) Complete decomposition of the hypervalent iodine reagents. d) 2.2 equiv. of **20** were required.

Other Lewis acid could be also used in this transformation, but with inferior results: TMSOTf gave the product in 16% yield only (table 1, entry 7); In the case of Cu(II) triflate, although a similar yield was obtained, significant decomposition of products **21** into *N*-methyl-3-iodo-indole was observed (table 1, entry 8). No product could be isolated with a silver(I) catalyst (table 1, entry 9). As fluoride-substituted benziodoxole reagents have been

successfully used as precursors in previous works,^[87] fluoride sources were then examined, but without success (table 1, entries 10 and 11). Finally, we decided to screen other solvents, as Zn(OTf)₂ was only scarcely soluble in Et₂O. When THF was used, no product was obtained probably due to the low solubility of benziodoxolone **20** in this solvent (table 1, entry 12). In DCM, full conversion was observed, but it required the use of two

equivalents of benziodoxolone **20** (table 2, entry 13). Full conversion and an excellent 97% yield could be obtained by raising the amount of zinc(II) triflate to 20 mol% (table 1, entry 14). The developed protocol based on the catalytic use of a relatively mild Lewis acid is noteworthy, as most syntheses of alkynyl, vinyl or aryl benziodoxolone reagents usually require a stoichiometric amount of strong Lewis or Brønsted acid.^[32,88,89] In fact, these reported procedures were not successful for the synthesis of IndoleBX **21**, as they led to complete decomposition of indole **14**. Furthermore, IndoleBX **21** displayed excellent thermal stability properties when compared to indole iodonium salts. A DSC measurement showed that significant decomposition started only at 151 °C, with a peak maximum at 183 °C (figure 2). An exothermic decomposition (283 J/g) was observed, with a peak height of 17.3 mW and a peak width of 3.7 °C.^[90]

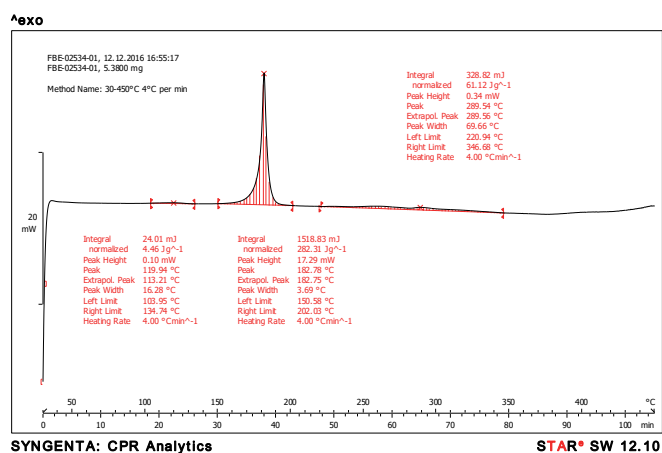


Figure 2. DSC measurement of IndoleBX **21**.

When the reaction was scaled up to 0.2 mmol, Indole-BX **21** was obtained in 87% yield (eq. 4)). No decrease in yield was observed when scaling up to 1-10 mmol (gram scale). The developed protocol could also be applied to benziodoxole reagents. The yield of hexafluoropropanol-derived benziodoxole **17** was also improved under these reaction conditions. The dimethyl reagent **23** was also synthesized in 51% yield. The developed reaction conditions could not be used for *N*-unprotected indoles. Nevertheless, the use of *N*-TBS protected indole (**24**) afforded a mixture of unreacted starting material, *N*-TBS protected reagent in low yield and a small amount of NH free indole reagent **25**. When 20 mol% of Sc(III) triflate was used instead, NH free reagent **25** could be obtained cleanly in 78% yield (eq. 5). Reagent **25** showed crystalline properties, unlike other reagents that presented a resin-like amorphous character. It was possible to obtain high quality crystal for X-ray analysis, which finally confirmed the hypervalent structure of the reagents (figure 3).

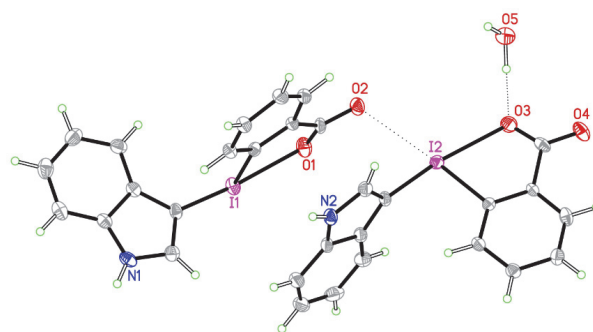
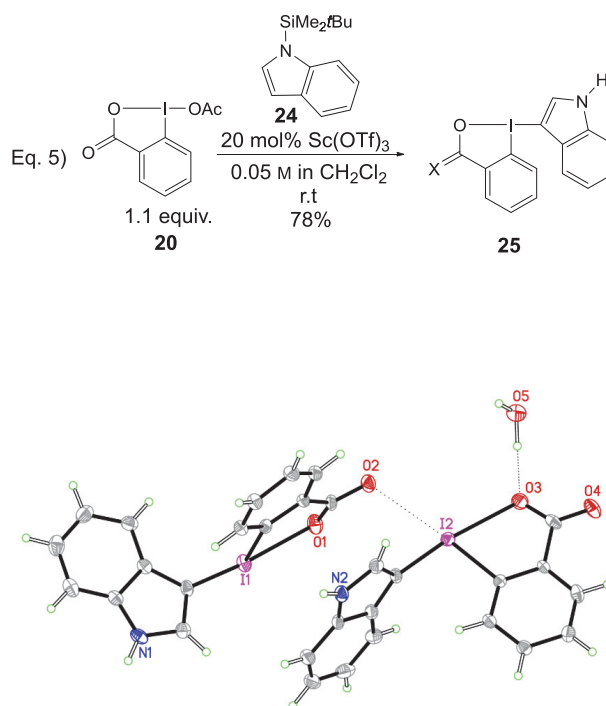
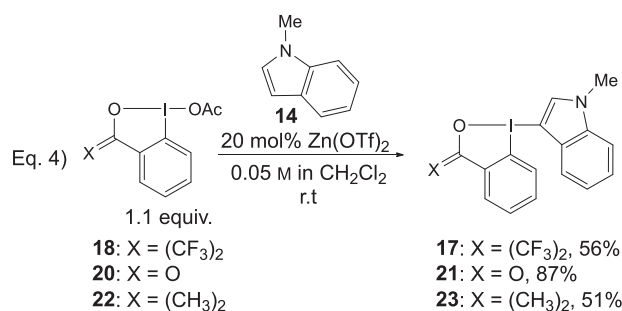


Figure 3. ORTEP drawing of reagent (**25**)·H₂O

The method proved to be reliable also in the synthesis of reagents bearing different functional groups on the indole ring (figure 4). In case of electron-donating functional groups such as methyl on the C2 position or methoxy on the C5 position, the respective reagents **26** and **27** were obtained in excellent yields. Halogen substituents were also tolerated under the reaction conditions: fluorine, chlorine and iodine containing reagents **28-30** were synthesized in 62-85% yield. With a pinacol boronate in C5 position, reagent **31** was obtained in moderate yield. The tolerance towards both halogen and boron substituents sets the stage for further functionalization via cross-coupling reactions. All these reagents could be synthesized on 1 mmol scale without the need for any re-optimization. We then investigated variation of the nitrogen substituent. Different alkyl chains were tolerated. While the *N*-phenyl-propyl reagent **32** and the *N*-3-butenyl reagent **33** were isolated in very good yields, the *N*-triisopropylethoxy **34** suffered from a slight decrease in yield.

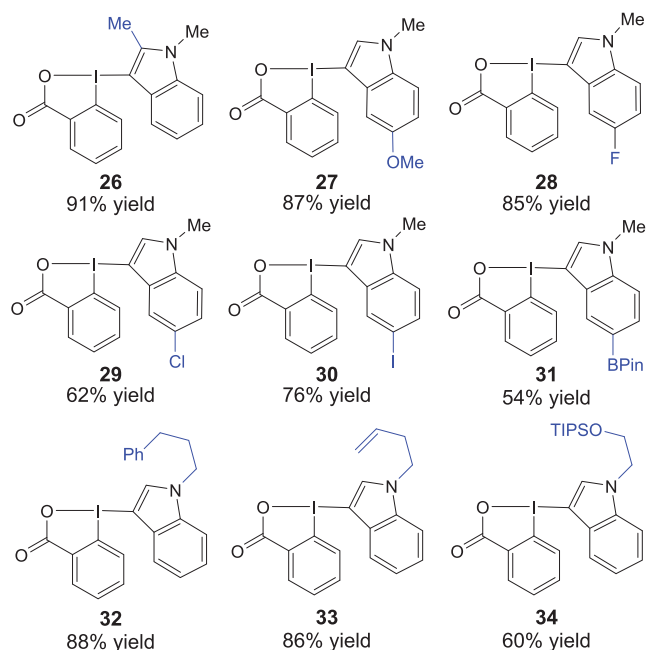


Figure 4. Scope of IndoleBXs: variation of the functional groups on indole. Reaction conditions: 1.00 mmol heterocycle, 1.10 mmol **20**, 0.200 mmol $\text{Zn}(\text{OTf})_2$, 0.05 M in CH_2Cl_2 , r.t., open air. Isolated yields.

The synthesis of PyrroleBX reagents was then investigated (figure 5). When *N*-methyl or *N*-benzyl pyrroles were employed as starting materials, separable regioisomeric C2:C3 mixtures of reagents **35** and **36** were obtained in high yield. In the case of **36**, the steric hindrance of the *N*-substituent led to the formation of the C3 isomer as the major one. The importance of steric effects was confirmed by the use of a *N*-TBS group which led to the formation of C3-substituted reagent **37** exclusively by using $\text{Sc}(\text{OTf})_3$ as catalyst. As in the case of indole reagent **25**, complete deprotection of the silyl group occurred. As for reagent **25**, reagent **37** showed good water solubility and crystalline properties. It was possible to obtain an X-ray analysis confirming the substitution at the C3 position (figure 6).

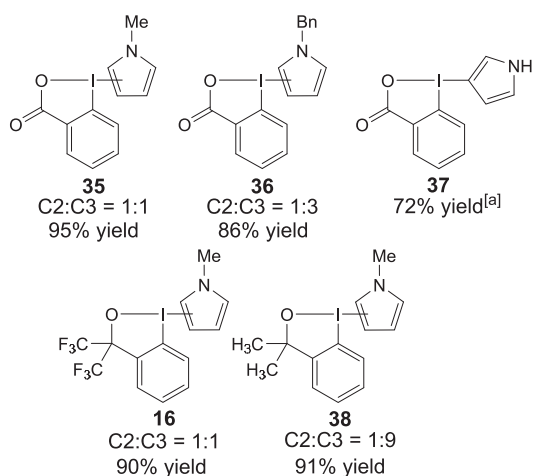


Figure 5. Scope of PyrroleBX reagents. Reaction conditions: 1.00 mmol heterocycle, 1.10 mmol **18**, **20** or **22**, 0.200 mmol $\text{Zn}(\text{OTf})_2$, 0.05 M in CH_2Cl_2 , RT, open air. Isolated yields. [a] $\text{Sc}(\text{OTf})_3$ was used starting from *N*-TBS-pyrrole (TBS = *tert*-butyldimethylsilyl).

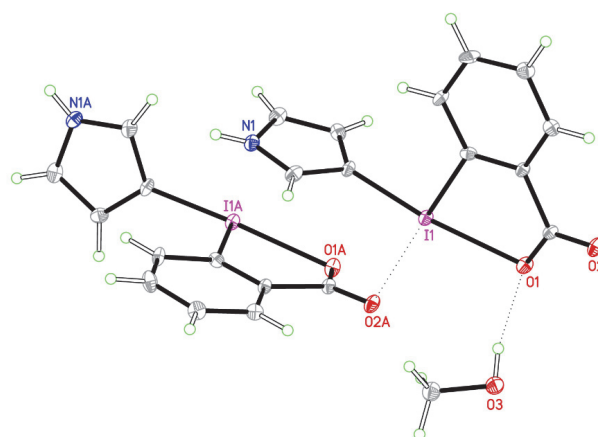


Figure 6. ORTEP drawing of reagent **37**·MeOH

We then investigated if the nature of the reagent backbone could influence the C2:C3 ratio for PyrroleBX reagents. When applying the optimized conditions to the synthesis of the hexafluorodimethyl-scaffold, reagent **16** was again formed as a 1:1 mixture of isomers. However, when we performed the reaction with dimethyl precursor **22**, benziodoxole **38** was obtained as an inseparable 1:9 mixture of C2:C3 regioisomers. At this point, the reasons for the higher regioselectivity observed with this reagent are not clear. One possible explanation would be lower electrophilicity at the iodine center, which would lead to steric effects dominating about the higher nucleophilicity of the C2 position.

In order to confirm this hypothesis, we decided to investigate the influence of electron-donating and electron-withdrawing groups when installed on the arene ring of the reagents (figure 7).^[82] IndoleBX **39** could be obtained in 56% yield. The corresponding PyrroleBX reagent **40** was formed as a 1:2 C2:C3 mixture of regioisomers. The ratio shifted slightly towards the less electron-rich and less encumbered C3 position when compared with reagent **35**. A fluorine in *meta* position to the iodine did not influence massively the outcome of the reaction, as **41** was obtained as a 1:3 ratio of C2:C3 isomers. Finally, with a strong electron-withdrawing nitro group in *para* position to the iodine, the ratio reversed in favor of the C2 regioisomer. The desired reagent **42** was obtained with a 4:1 C2:C3 ratio in excellent yield. In this case, the iodine atom was expected to be highly electrophilic and electronic control would become more important than sterics.

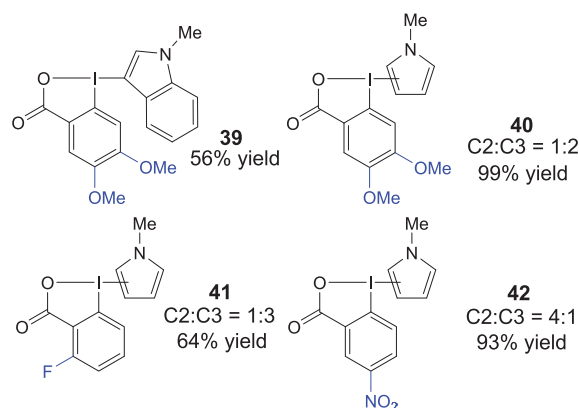


Figure 7. Scope of IndoleBXs and PyrroleBXs: modification of the benzene ring. Reaction conditions: 0.20 mmol heterocycle, 0.220 mmol acetoxybenziodoxolone, 0.040 mmol $\text{Zn}(\text{OTf})_2$, 0.05 M in CH_2Cl_2 , RT, open air. Isolated yields.

Finally, preliminary investigations were done for the synthesis of reagents bearing other heterocycles than indole or pyrrole (figure 8). Azaindole-based reagent **43** was obtained in moderate yield and high C3 regioselectivity. In case of CarbazoleBX **44**, the yield was moderate, but the regioselectivity very high, as the iodine was bound exclusively to the carbon in *para* position to the nitrogen. ThiopheneBX **45** and DimethylFuranBX **46** were also synthesized in low to moderate yield. In this case, the corresponding iodonium salts are already known and have been applied in catalytic transformations.^[91–96]

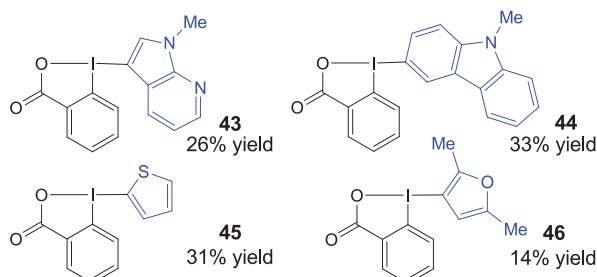
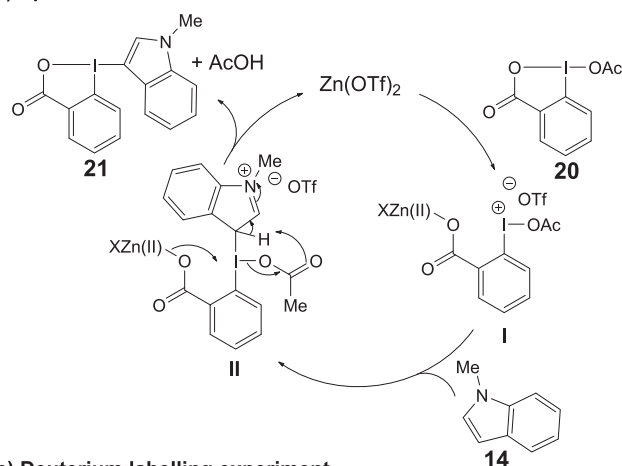


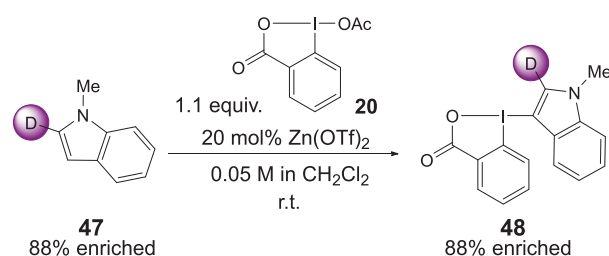
Figure 8. Scope of other HeterocyclicBXs. Reaction conditions: 1.00 mmol heterocycle, 1.10 mmol **20**, 0.200 mmol Zn(OTf)₂, 0.05 M in CH₂Cl₂, RT, open air. Isolated yields.

At this point only a highly speculative mechanism can be proposed for the formation of the IndoleBX reagents (scheme 3a). Activation of benzodioxole **20** by zinc(II) triflate would first give highly electrophilic iodonium intermediate **I**.^[84] Nucleophilic attack of *N*-methyl indole (**14**) on the iodine center will then give intermediate **II**. The acetate ligand could then act as an internal base to re-aromatize the indole ring, leading to the formation of acetic acid and closing of the benzodioxole ring. Activation of the acetate as a leaving group by zinc(II) triflate followed by the acetate acting as an external base could also be considered. In previous mechanism studies involving the activation of heterocycles with hypervalent iodine reagents, the formation a charge-transfer (CT) complex between the hypervalent iodine reagent and the heterocycle had been proposed.^[97,98] Single electron transfer would then give a radical cation intermediate that would recombine with the formed iodine radical. This mechanism appeared less probable to rationalize the formation of IndoleBX **21**, based on the fact that (1) Moriarty and co-workers had observed a fast fragmentation of the radical formed from indole iodonium salt to give 3-iodo-indole and the benzene radical;^[39] No 3-iodo indole was observed in our work; And (2) the high selectivity observed for the C3 position is difficult to rationalize for a radical pathway. Formation of a C2-bond iodine intermediate followed by migration can also be excluded, as the C2-enriched deuterium reagent **48** was obtained without the loss of any deuterium enrichment (scheme 3b).

a) Speculative mechanism

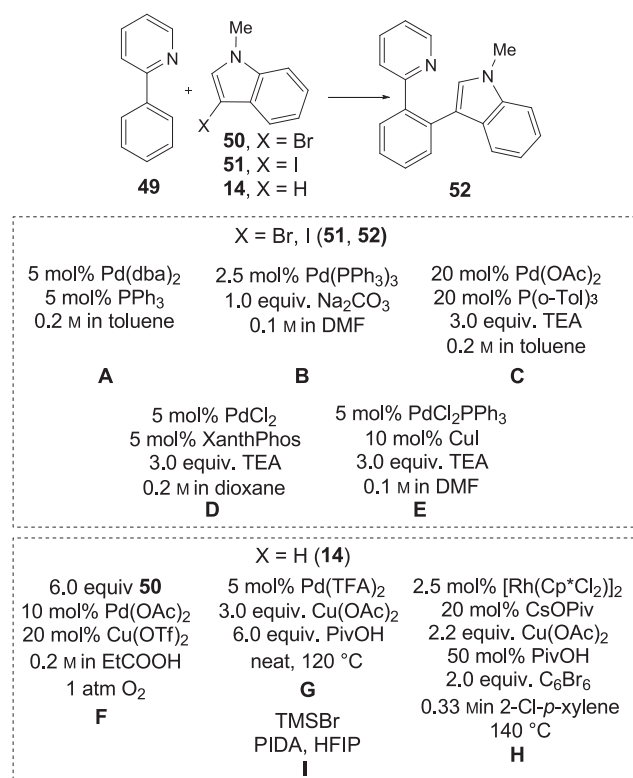


b) Deuterium labelling experiment



Scheme 3. Speculative mechanism and deuterium labelling experiment. For simplification, the exact geometry at the iodine center including the lone pairs is not drawn.

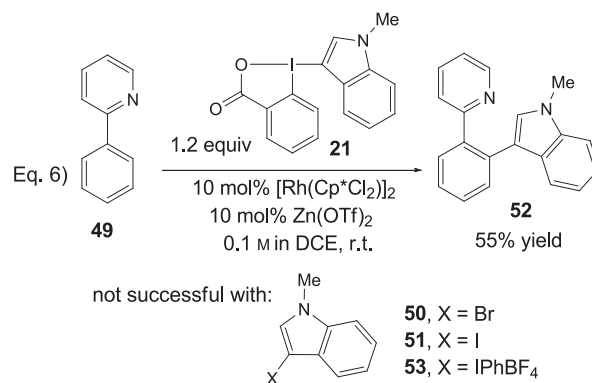
With a broad range of new IndoleBX and PyrroleBX in hand, we started investigating possible applications. As previously stated in the introduction, arylated pyrroles and indoles constitute a class of versatile molecules, but their synthesis based on arene C-H functionalization has not been realized so far. In particular, (hetero)-arylated aryl-pyridines such as **52** (scheme 4) would be useful as key intermediates for the synthesis of optoelectronic materials.^[99] However, no synthesis via direct *ortho* C-H functionalization has ever been reported, despite the tremendous recent progress in this area.^[100] We first investigated if the indolation of pyridine **49** would be possible using state-of-the-art C-H functionalization methods (scheme 4). Reported catalytic systems based on palladium(0) (**A**, **B**)^[101,102] or palladium(II) (**C**, **D**)^[59,103] precursors in combination with iodo- and bromo-indoles, did not lead to the formation of the desired product **52**. Using a palladium(II)/copper(I) mixed system was also unsuccessful (**E**).^[102] Oxidative methods reported for the direct C-H coupling of indoles were then examined. However, neither palladium (**F**, **G**)^[18,104] or rhodium (**H**)^[105]-based methods, nor direct oxidation with hypervalent iodine reagents activated by Lewis acids (**I**)^[92] worked efficiently. All the reported catalytic methods were screened at different temperatures, starting from 50 °C and increasing up to a maximum of 140 °C, in order to take into account different reaction kinetics.



Scheme 4. Attempted synthesis of 2-indolyl pyridine **52** using reported C-H functionalization methods.

We then turned to the use of the new Indole-BX reagent **21**. Although no product could be obtained using reported palladium-catalyzed protocols (**A-E**, scheme 4), **52** was obtained in 55% yield when using the mild conditions developed by Li and coworkers for the rhodium-catalyzed alkylation of arenes with EBX reagents (Eq. 6).^[52] The product was

obtained as a single C3 regioisomer with complete chemoselectivity, as the benzoate group was not transferred on the aryl-pyridine. This is noteworthy, as controlling the selectivity of aryl transfer from iodonium salts is generally challenging.^[106] Furthermore, transfer of the benzoic acid is usually observed in the reaction of aryl benziodoxolones with nucleophiles.^[89] Under these conditions, no product was obtained with either iodo- or bromo- indoles **50** and **51**. Indolyl benzyl iodonium salt **53**^[35] was also not successful.



Based on this promising result (table 2, entry 1), we started to optimize the transformation. First, control experiments showed that no reaction occurred with Lewis acids only (table 2, entry 2), even using the conditions specifically developed by Kita and coworkers for the activation of hypervalent iodine reagents (TMSBr in HFIP, table 2, entry 3).^[92] Several solvents were then screened (table 2, entries 4-7). In DCM, a lower yield was obtained (table 2, entry 4) and no product was observed in methanol or toluene (table 2, entries 5 and 6). In DMF a good 66% yield of **52** was obtained, but only upon heating at 110 °C (table 2, entry 7).

Table 2. Optimization of the C-H indolation of pyridine **50**.

Entry	Solvent (M)	Base (mol%)	Additive (mol%)	Rh (mol%)	T (°C)	Yield %*
1	DCE	-	Zn(OTf) ₂ (10)	[Rh(Cp*Cl ₂) ₂] (5)	RT	55%
2	DCE	-	Zn(OTf) ₂ (10)	-	RT	-
3	HFIP	-	TMSBr	-	RT	-
4	DCM	-	Zn(OTf) ₂ (10)	[Rh(Cp*Cl ₂) ₂] (5)	RT.	25%
5	MeOH	-	Zn(OTf) ₂ (10)	[Rh(Cp*Cl ₂) ₂] (5)	RT	-
6	Toluene	-	Zn(OTf) ₂ (10)	[Rh(Cp*Cl ₂) ₂] (5)	RT	-
7	DMF	-	Zn(OTf) ₂ (10)	[Rh(Cp*Cl ₂) ₂] (5)	110	66%
8	DCE	K ₂ CO ₃ (10)	-	[Rh(Cp*Cl ₂) ₂] (5)	RT	28%

9	DCE	KOAc (10)	-	[Rh(Cp*Cl ₂) ₂] (5)	RT	37%
10	DCE	KOPiv		[Rh(Cp*Cl ₂) ₂] (5)	RT	49%
11	DCE	NaOAc (10)	-	[Rh(Cp*Cl ₂) ₂] (5)	RT	69%
12	DCE	NaOPiv (10)	-	[Rh(Cp*Cl ₂) ₂] (5)	RT	72%
13	DCE	-	AgNTf ₂ (10)	[Rh(Cp*Cl ₂) ₂] (5)	RT	- ^b
14	DCE		AgSbF ₆ (10)	[Rh(Cp*Cl ₂) ₂] (5)	RT	17%
15	DCE	NaOPiv (10)	AgSbF ₆ (10)	[Rh(Cp*Cl ₂) ₂] (5)	RT	90%
16	DCE	NaOPiv (10)	AgSbF ₆ (10)	[Rh(Cp*Cl ₂) ₂] (2.5)	RT	78%
17	DCE	NaOPiv (10)	AgSbF ₆ (10)	[Rh(Cp*Cl ₂) ₂] (2.5)	50	82%
18	DCE	NaOPiv (10)	AgSbF ₆ (10)	[Rh(Cp*Cl ₂) ₂] (1.25)	50	37%

a) Pyridine **49** (0.100 mmol), IndoleBX **21** (0.110 mmol), [Rh(Cp*Cl₂)₂] (X mol%), base (X mol%), additive (X mol%) and solvent (0.1 M) at T °C. Isolated yield after flash chromatography is given. b) Decomposition of the hypervalent iodine reagent **21** was observed.

To further facilitate a possible CMD (concerted metalation-deprotonation) at room temperature, we then screened carbonate and carboxylate salts instead of zinc(II) triflate.^[107] While potassium salts gave moderate yields (table 2, entries 8-10), sodium salts worked better. NaOAc afforded **52** in 69% yield and NaOPiv in 72% yield (table 2, entries 11-12). As Ag(I) salts are known to play a pivotal role in activating the catalyst by chloride abstraction to give ionic active species,^[108] AgNTf₂ and AgSbF₆ were then examined as additive. In absence of a base, the former led to decomposition of the hypervalent iodine reagent **21**, whereas the latter gave the desired product in 17% only (table 2, entries 13 and 14). Nevertheless, the combination of carboxylate bases and AgSbF₆ increased the yield up to 90% (table 2, entry 15). Lowering the catalyst to 2.5 mol% unfortunately led to lower yield at room temperature (table 2, entry 16), but 82 % could be obtained when the temperature was increased to 50 °C (table 2, entry 17). When further lowering the catalyst loading, no full conversion could be obtained (table 2, entry 18).

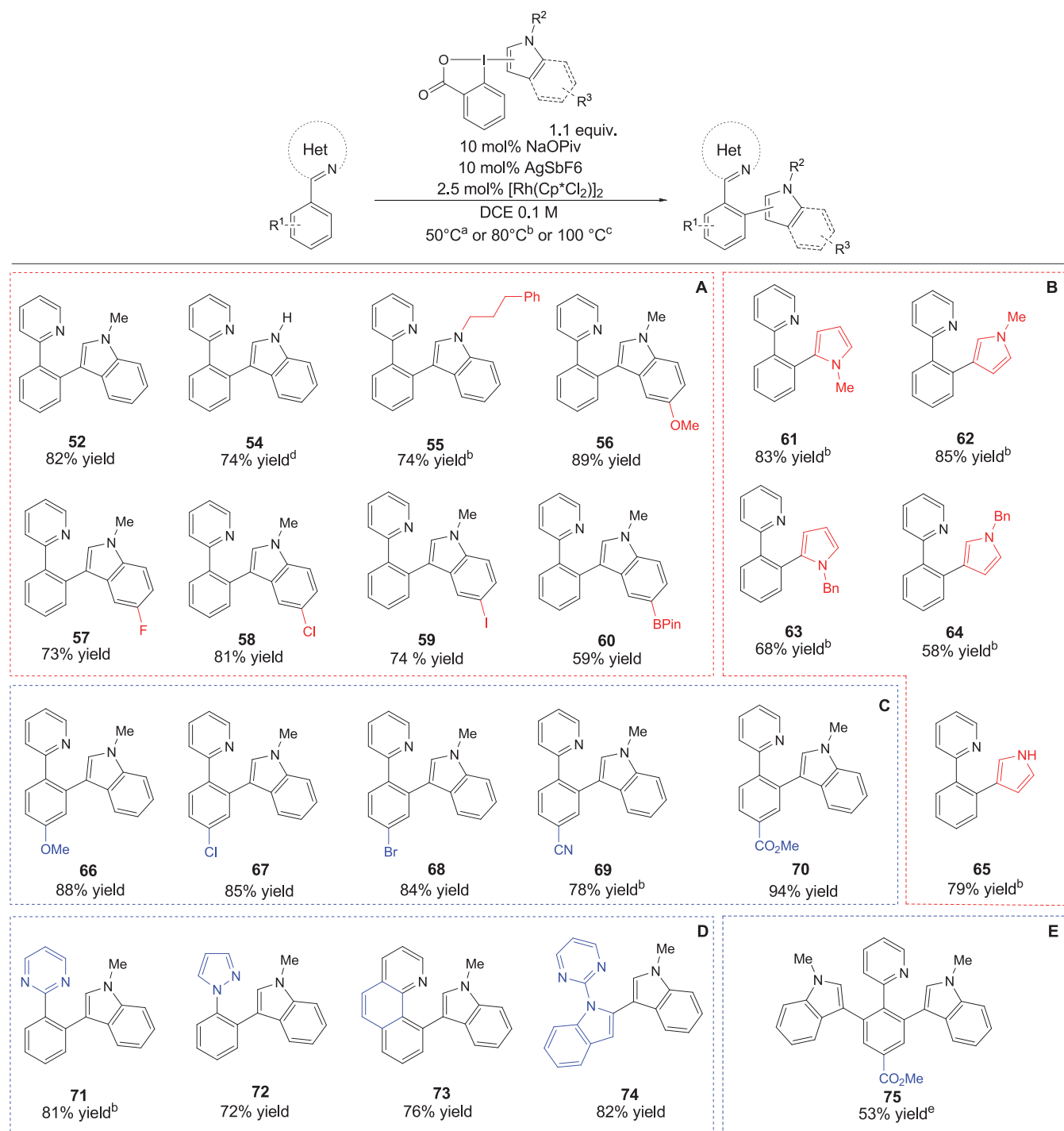
We then proceeded with the investigation of the scope of the new C-H functionalization (scheme 5). Differently substituted IndoleBX were first used and gave the desired heteroarylated-arylpyridines in very good yields (scheme 5A). In particular, NH-free indole product **54** could be accessed in 74%, provided methanol was used as co-solvent for enhancing the solubility. A larger alkyl substituent on the nitrogen was also well tolerated (product **55**). On the C5-indole position, an electron-donating methoxy group as well as electron-withdrawing halogens were well tolerated, and the products **56-59** were isolated in 74-89% yields. We were also delighted to see that the pinacol boronate group was compatible with our method, as boronic ester **60** could be accessed in 59% yield. When different PyrroleBX reagents were employed, the regioselective synthesis of products **61-65** became possible based on the availability of the pure reagent isomers (scheme 5B). In this case again, it was possible to access N unprotected pyrrole **65** in 79% yield. The presence of various functional groups on the aryl-pyridine substrate was then investigated (scheme 5C).

Again, methoxy and halogen groups were well tolerated (products **66-68**).

We were pleased to see that a cyano group could also be introduced, as **69** was obtained just by increasing the temperature to 80 °C. Ester **70** was formed in nearly quantitative yield. Different other heterocyclic directing groups such as pyrimidines, pyrazoles and benzoquinolines could also be used (scheme 5D): products **71-73** were obtained in 72-81% without the need for re-optimization of the reaction conditions. A pyrimidine directing group could also be used for the synthesis of C2-C3 indole dimer **74**. Finally, with the double amount of IndoleBX **21**, di-indolated product **75** was isolated in 53% yield (scheme 5E).

Quinolones and purines are other classes of important heterocycles in bioactive compounds. As shown in Figure 9, quinolone **76** could be synthesized in 38% yield. In this case, quinoline N-oxide was used as starting material. Functionalized purine base-containing nucleoside **77** could be also obtained via C-H functionalization in 41% yield.^[109]

The obtained C-H functionalization products based on heterocyclic directing groups are highly useful building blocks for medicinal chemistry or organic materials. Nevertheless, they constitute “synthetic end points”, as the directing group cannot be easily removed. In order to enhance the synthetic versatility of the new C-H arylation, we therefore turned to the recently developed ruthenium catalyzed C-H functionalization of arenes using methoxy-amides directing groups (scheme 6).^[56] This directing group is simple to install and easily transformable. Moreover, ruthenium is a cheaper and more abundant metal. In this case, similar targeted products were already synthesized in the past, but only via cross-coupling reactions requiring pre-functionalization of the arene ring.^[110] Gratifyingly, when the conditions developed by Cheng and coworkers for C-H alkynylation with EBX reagents^[56] were used with amide **78** and IndoleBX **21**, the desired product **79** was obtained in 55% yield (scheme 6). Control experiments showed that no direct C-H coupling with *N*-methyl indole (**14**) was feasible under palladium- or rhodium-catalyzed conditions reported for this substrate (scheme 6, conditions A-C).^[18,105,111]



Scheme 5. Scope of the Rh-catalyzed C-H (hetero)arylation. a) Reaction conditions: substrate (0.300 mmol), reagent (0.330 mmol), [Rh(Cp*Cl₂)₂] (2.5 mol%), NaOPiv (10 mol%), AgSbF₆ (10 mol%) and DCE (0.1 M) at 50 °C. Isolated yields. b) At 80 °C. c) At 100 °C. d) 0.1 M in DCE:MeOH (1:1 ratio). e) 0.660 mmol of IndoleBX **21** were used.

Based on this promising result, the ruthenium-catalyzed C-H indolation of benzamide **78** was further optimized. Screening of solvent showed the importance of a fluorinated alcohols, as methanol and ethanol led to lower yield of **79** (table 3, entries 1-3). Chlorinated solvents that worked well for the rhodium-catalyzed process such as DCM and DCE did not afford any conversion (table 3, entry 4). The choice of the base was also fundamental: sodium carboxylate bases gave the best result (table 3, entries 5-6), but none of the simple carboxylates initially tested were superior to sodium acetate (table 3, entry 1). The corresponding potassium salts gave inferior results (table 3, entries 7-9). Based on these initial results, we decided to

screen further sodium carboxylate salts (table 3, entries 10-13). While sodium benzoate (**80**) led to no conversion (table 3, entry 10). Adamantane-, xanthene- and diphenyl-based carboxylate salts **81-83** afforded the desired compound **79** in 65-68% yield (table 3, entries 11-13). Although the three bases **81-83** afforded similar yields, adamantyl-carboxylate base **81** led to a cleaner reaction profile. Different Ag(I) salts were also screened to further activate the catalyst,^[82] but they prevented the reaction to occur (table 3, entry 14).

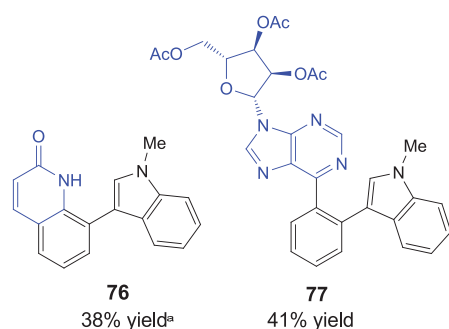
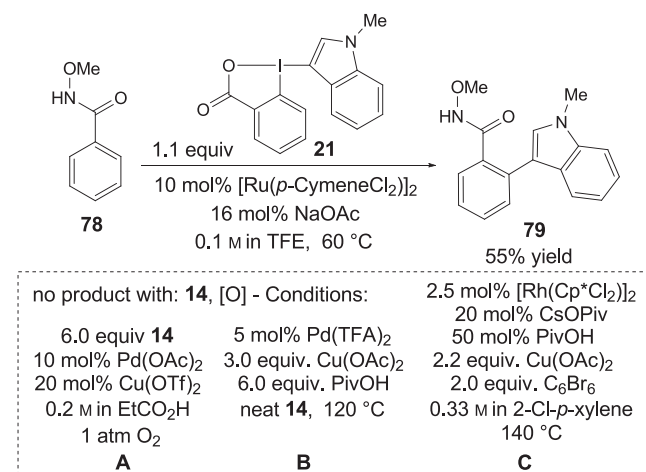


Figure 9. Indole-substituted quinolones and purines obtained by the Rh-catalyzed C-H functionalization with IndoleBX **21**. Reaction conditions: Substrate (0.300 mmol), Indole source (0.330 mmol), [Rh(Cp*Cl₂)₂] (2.5 mol%), NaOPiv (10 mol%), AgSbF₆ (10 mol%) and DCE (0.1 M) at 50 °C. Isolated yields. a) At 100 °C.

Finally, the expected active catalyst **84** was synthesized^[112] and used in the reaction (table 3, entry 15). A similar result was obtained, but the protocol was more user friendly, as all reaction components could be added at the same time, only one degassing cycle had to be performed and no pre-mixing was required. Moreover, the active complex was perfectly soluble in the reaction medium, allowing us to work under homogeneous condition.

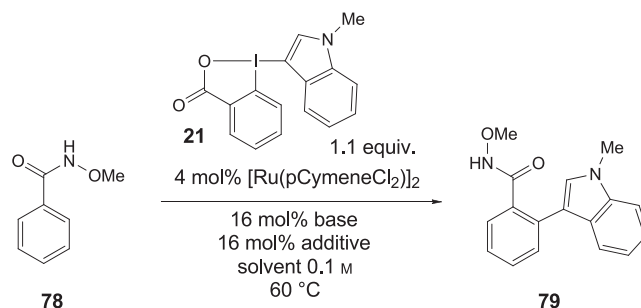
We then performed preliminary investigations on the scope of the new ruthenium-catalyzed C-H indolation, focusing this time on functional group substitution of the arene ring (figure 10). Substitution in *para* position to the amide was possible with both electron-rich (products **85**

and **86**) and electron-poor (products **87** and **88**) substituents. A broad range of substituents was also tolerated in *meta* position (products **89-92**). Double-substitution in both positions was also possible (product **93**). Functionalized naphthyl amide **94** could also be obtained in 79% yield. The fast synthesis of halogenated arenes is especially interesting for application in medicinal chemistry, either for further functionalization via cross-coupling reactions, or due to the interesting properties of fluorine in drugs, especially for blocking metabolism and increasing lipophilicity.



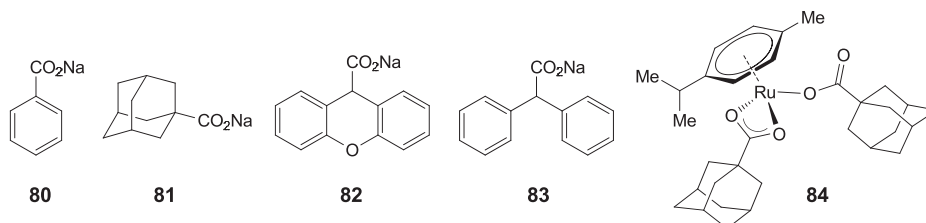
Scheme 6. Lead result for the Ru-catalyzed C-H indolation and control experiments.

Table 3. Optimization of the ruthenium-catalyzed C-H indolation.



Entry	Solvent (M)	Base (mol%)	Additive (mol%)	Ru (mol%)	Yield % ^a
1	TFE	NaOAc (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	55%
2	MeOH	NaOAc (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	43%
3	EtOH	NaOAc (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	34%
4	DCM/DCE	NaOAc (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	-
5	TFE	NaOPiv (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	50%
6	TFE	MesCOONa (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	34%
7	TFE	KOAc (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	-
8	TFE	KOPiv (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	-
9	TFE	MesCOOK (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	26%
10	TFE	80 (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	-
11	TFE	81 (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	68%
12	TFE	82 (16)	-	[Ru(<i>p</i> -CymeneCl ₂) ₂] ₂ (4)	65% ^b

13	TFE	83 (16)	-	$[\text{Ru}(p\text{-CymeneCl}_2)]_2$ (4)	66% ^b
14	TFE	81 (16)	Ag(I)X (16)-	$[\text{Ru}(p\text{-CymeneCl}_2)]_2$ (4)	-
15	TFE	-	-	84 (10)	68%



a) Substrate **78** (0.100 mmol), IndoleBX **21** (0.110 mmol), $[\text{Ru}(p\text{-CymeneCl}_2)]_2$ (X mol%), base (X mol%), additive (X mol%) and solvent (0.1 M) at T °C. Isolated yield after flash chromatography is given. b) Decomposition was observed.

Conclusions

In this work, a full account of the synthesis of the hypervalent iodine reagents IndoleBX and PyrroleBX as a novel class of bench-stable electrophilic indole and pyrrole equivalents and their application in Rh(III) and Ru(II) catalyzed C-H (hetero)arylation of different arenes is described. In total 33 new hypervalent iodine reagents are reported. A broad range of different substituents could be introduced on the heterocycle and on the reagents backbone. *N*-Methyl-IndoleBX **21** was accessible on gram scale and presents high thermal stability. Based on the use of these new reagents, indoles and pyrroles were transferred directly on the C-H bond of various arenes in a mild, chemo- and regio-selective fashion. While Rh(III) was employed in combination with a heterocyclic nitrogen donor directing group, Ru(II) enabled the functionalization of versatile aryl-methoxamides. The two methods were robust, and a broad scope was obtained as several functional groups were well tolerated. The synthesis and novel applications of heterocyclic-based hypervalent iodine reagents has just started in our laboratory and important progress can be expected in the future.

Supplementary Material

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/MS-number>.

Acknowledgements

This work is supported by the Swiss National Science Foundation (No. 200021 159920), the European Research Council (ERCStarting Grant 334840) and the COST action CA15106 (C-H Activation in Organic Synthesis, CHAOS). We thank Dr R. Scopelliti and Dr F. F. Tirani from ISIC at EPFL for X-ray analysis, and Dr. Fides Benfatti and Ms. Marylene Stempien from Syngenta CropScience for DSC experiments. Dr. Stefano Nicolai from EPFL is thanked for revising the manuscript.

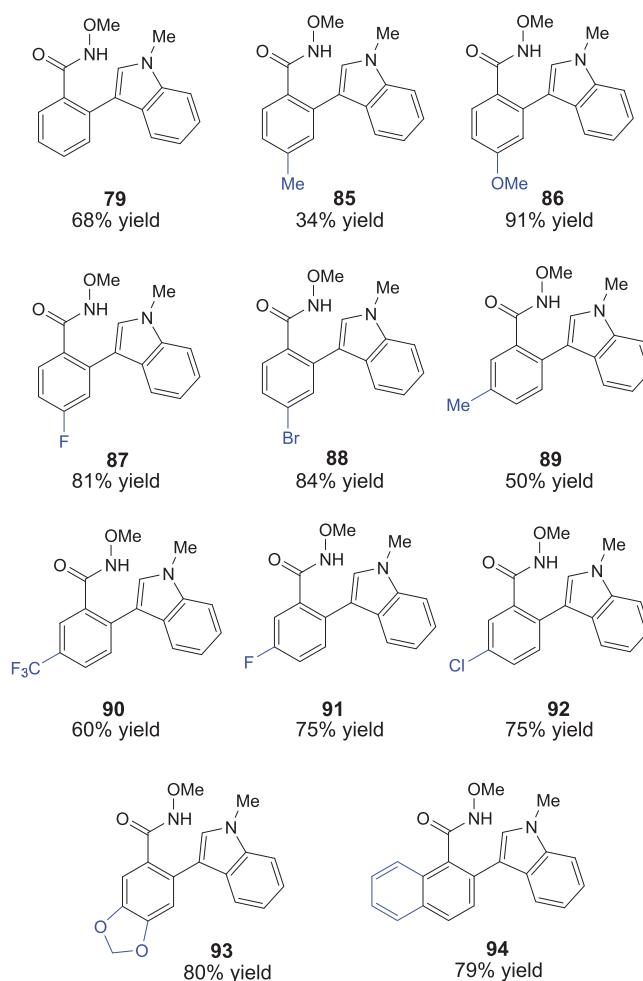


Figure 10. Scope of the Ru-catalyzed C-H (hetero)arylation. Reaction conditions: Substrate (0.300 mmol), IndoleBX **21** (0.330 mmol), **84** (10 mol%), and TFE (0.1 M) at 60 °C.

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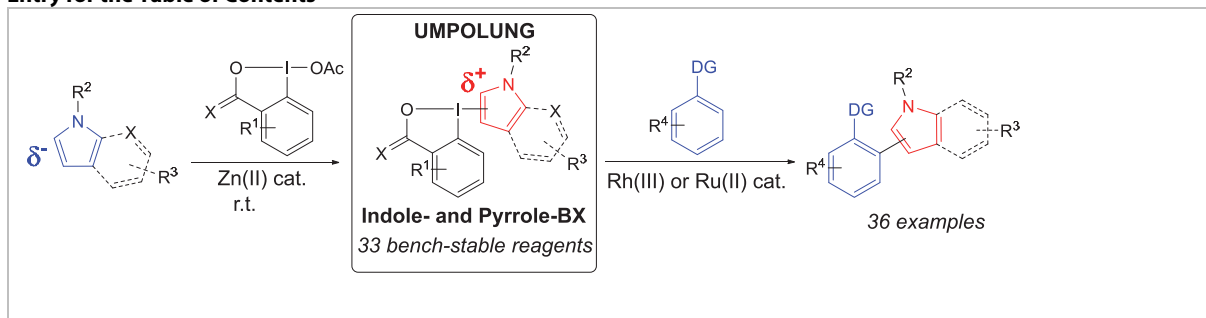
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Entry for the Table of Contents



Supplementary Materials for

**Bench-Stable Electrophilic Indole and Pyrrole Reagents:
Serendipitous Discovery and Use in C-H Functionalization**

Paola Caramenti and Jerome Waser

Supporting Information

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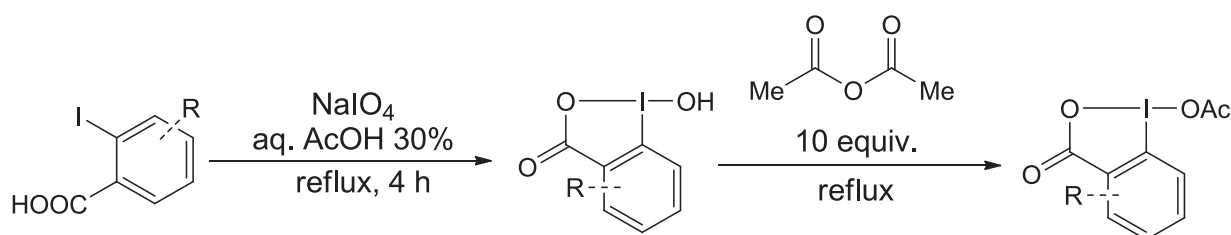
1. Materials and Methods.

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography, technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et₂O, CH₃CN, toluene, hexane and CH₂Cl₂ were dried by passage over activated alumina under nitrogen atmosphere (H₂O content < 10 ppm, *Karl-Fischer* titration). The solvents were degassed through Freeze-Pump-Thaw method when mentioned. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem, or Merck and used as such unless otherwise stated. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, with the solvents indicated as eluent under 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F₂₅₄ TLC glass plates or aluminium plates and visualized with UV light, permanganate stain, CAN stain, or Anisaldehyde stain. Melting points were measured on a Büchi B-540 melting point apparatus using open glass capillaries, the data is uncorrected. ¹H-NMR spectra were recorded on a Bruker DPX-400 400 MHz spectrometer in CDCl₃, DMSO-*d*₆, CD₃OD, C₆D₆ and CD₂Cl₂, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm the internal methanol signal at 3.30 ppm, the internal dichloromethane signal at 5.30 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation). ¹³C-NMR spectra were recorded with ¹H-decoupling on a Bruker DPX-400 100 MHz spectrometer in CDCl₃, DMSO-*d*₆, CD₃OD or CD₂Cl₂, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal DMSO signal at 39.5 ppm, the internal methanol signal at 49.0 ppm and the internal dichloromethane signal at 54.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm⁻¹ (w = weak, m = medium, s = strong, br = broad). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API.

2. Preparation of PyrroleBXs and IndoleBXs.

The synthesis of the precursors for HeterocyclicBX reagents **21**, **25**, **26-37**, **43-46** and their starting materials had been already described before.^[1,2] The procedures here reported are taken from the cited publications to facilitate reproduction of the results by having all the data in the same file.

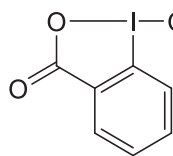
2.1 Preparation of Hypervalent Iodine Precursors.



Following a reported procedure,^[1] NaIO_4 (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acids (8.00 g, 32.2 mmol, 1.00 equiv) were suspended in 30% (v/v) aq. AcOH (48 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to room temperature, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 20 mL) and acetone (3 x 20 mL), and air-dried in the dark to give the pure hydroxylated intermediates.

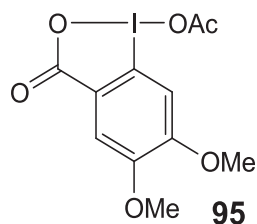
Following a reported procedure,^[2] hydroxylated intermediates (39.1 mmol, 1.00 equiv.) were suspended in acetic anhydride (35 mL) and heated to reflux for 30 minutes. The resulting clear, slightly yellow solution was slowly let to warm up to room temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 20 mL) and dried *in vacuo* to afford products **20**, **95-97**.

1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one **20**



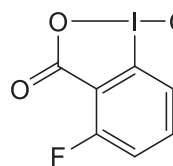
1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one **20** (10.8 g, 35.3 mmol, 90%) as a white solid. ^1H NMR (CDCl_3 , 400 MHz) δ 8.24 (dd, $J = 7.6, 1.6$ Hz, 1H, Ar*H*), 8.00 (dd, $J = 8.3, 1.0$ Hz, 1H, Ar*H*), 7.92 (ddd, $J = 8.4, 7.2, 1.6$ Hz, 1H, Ar*H*), 7.71 (td, $J = 7.3, 1.1$ Hz, 1H, Ar*H*), 2.25 (s, 3 H, COCH_3). ^{13}C NMR (CDCl_3 , 100 MHz) δ 176.5, 168.2, 136.2, 133.3, 131.4, 129.4, 129.1, 118.4, 20.4. NMR values are in accordance with the data reported in literature.^[3]

5,6-Dimethoxy-3-oxo-1 λ_3 -benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**95**)



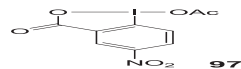
5,6-Dimethoxy-3-oxo-1 λ_3 -benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate **95** (12.8 g, 35.0 mmol, 89%) was obtained as a white solid. ^1H NMR (CDCl_3 , 400 MHz) δ 7.63 (s, 1H, Ar*H*), 7.36 (s, 1H, Ar*H*), 4.02 (s, 3H, OMe), 4.00 (s, 3H, OMe), 2.24 (s, 3H, OAc). ^{13}C NMR (CDCl_3 , 100 MHz) δ 176.4, 168.4, 155.9, 152.0, 121.8, 113.6, 110.0, 109.0, 56.6, 20.4. NMR values are in accordance with the data reported in literature.^[4]

4-Fluoro-3-oxo-1 λ_3 -benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**96**)



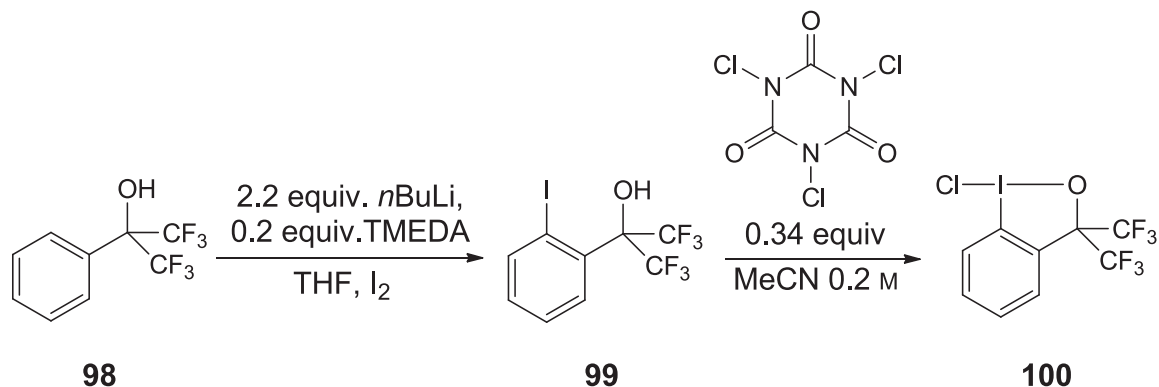
4-Fluoro-3-oxo-1 λ_3 -benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate **96** (9.62 g, 29.7 mmol, 76%) was obtained as a white solid. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.94 (td, $J = 8.2, 4.7$ Hz, 1H, Ar*H*), 7.73 (d, $J = 8.2$ Hz, 1H, Ar*H*), 7.62 (dd, $J = 10.3, 8.2$ Hz, 1H, Ar*H*), 2.24 (s, 3H, OAc). ^1H -NMR values are in accordance with the data reported in literature.^[4]

1-Acetoxy-5-nitro-1,2-benziodoxol-3(1*H*)-one ANBX (**97**)



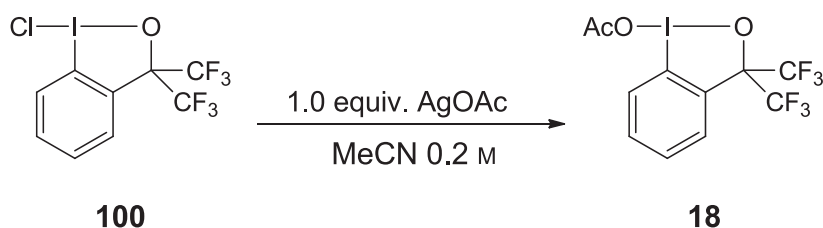
1-Acetoxy-5-nitro-1,2-benziodoxol-3(1*H*)-one **97** (8.71 g, 24.8 mmol, 64%) was obtained as a white solid. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.71 (dt, $J = 8.9, 2.7$ Hz, 1H, Ar*H*), 8.62 – 8.54 (m, 1H, Ar*H*), 8.12 (dd, $J = 23.8, 8.8$ Hz, 1H, Ar*H*), 1.90 (s, 3H, OAc). ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 172.0, 166.0, 149.8, 133.5, 128.3, 128.2, 127.8, 124.9, 21.1. NMR values are in accordance with the data reported in literature.^[5]

1-Chloro-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (100)



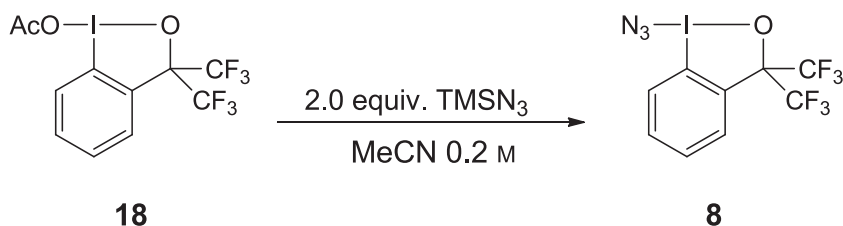
Following a reported procedure, TMEDA (distilled over KOH) (1.26 mL, 8.20 mmol, 0.200 equiv) was added to a solution of *n*BuLi (2.5 M in hexanes, 36.6 mL, 91.6 mmol, 2.20 equiv). After 15 min, the cloudy solution was cooled to 0 °C and **98** (7.00 mL, 42.0 mmol, 1 equiv) in THF (6 mL) was added dropwise. The reaction was stirred 30 min at 0 °C and then at RT overnight. I_2 (11.2 g, 44.0 mmol, 1.06 equiv) was then added portionwise at 0 °C and the mixture stirred at 0 °C for 30 min and 4 h at RT. The reaction was quenched with saturated NH_4Cl . Et_2O (100 mL) was added and the layers were separated. The aqueous layer was then extracted twice with Et_2O (3 x 50 mL). The organic layers were combined, washed twice with saturated $Na_2S_2O_3$ (2 x 50 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 15.6 g of crude **99** as a brown oil which was used without further purification. The crude oil was dissolved in MeCN (40 mL) in the dark under air. Trichloroisocyanuric acid (3.42 g, 14.3 mmol, 0.340 equiv.) was then added portionwise at r.t. After 30 min, the resulting suspension was filtered to afford **100** (7.30 g, 18.1 mmol, 43%) as a yellow solid. The mother liquors were carefully reduced to one third and filtered to afford more **100** (8.85 g, 21.9 mmol, 52.1% yield) as a yellow solid. **Mp**: 167 – 169 °C. 1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, 1 H, $J = 8.4$ Hz, ArH), 7.85 (m, 1 H, ArH), 7.73 (m, 2 H, ArH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.8, 132.1, 131.6, 129.7, 128.5, 122.8 (q, 289 Hz), 113.4, 84.8. The melting point and the 1H NMR correspond to the reported values.^[6]

1-Acetoxy-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (18)



1-Chloro-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole **100** (8.85 g, 21.9 mmol) and AgOAc (3.65 g, 21.9 mmol, 1 equiv.) were suspended in MeCN (109 mL, 0.2 M). After being stirred overnight in the dark, AgCl precipitated and was filtered off. The residue was washed with MeCN. The solvent was removed in vacuo to give **18** (9.37 g, 21.9 mmol, 100%) as a white solid. ¹H NMR (300 MHz, CDCl₃) δ 7.93 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.61–7.79 (m, 3H, Ar*H*), 2.18 (s, 3H, CH₃). The NMR values correspond to the reported ones.^[3]

1-Azido-3,3-bis(trifluoromethyl)-3-(1*H*)-1,2-benziodoxole (8).

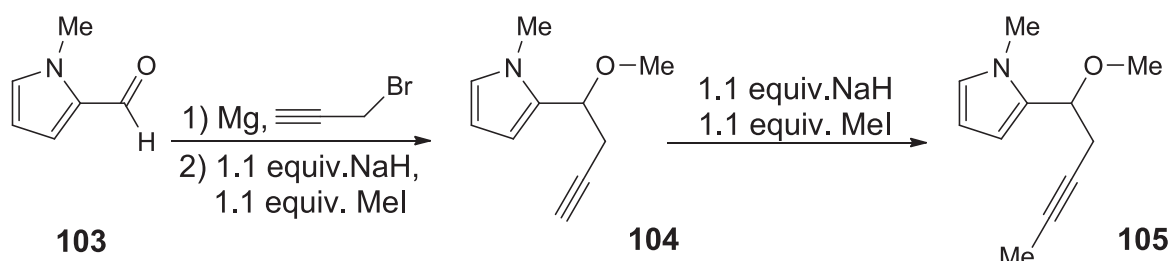


To a stirred mixture of 1-hydroxy-3,3-bis(trifluoromethyl)-3-(1*H*)-1,2-benziodoxole **18** (1.00 g, 2.60 mmol) in dry CH₃CN (20 mL) was added trimethylsilylazide (0.700 mL, 5.20 mmol) under nitrogen at room temperature. The reaction mixture was stirred for 18 h, and then the resulting yellow solution was evaporated in vacuum to give **8** as a pale crystalline solid (890 mg, yield 0.490 g (92%); mp 147–150 °C (from CH₃CN); IR ν 3076, 2048. ¹H NMR (CDCl₃:CD₃CN 10:1) δ 7.89–7.66 (m, 4H, Ar*H*). The IR and NMR values correspond to the reported ones.^[7]

2.2 Preparation of the Starting Materials for the Synthesis of PyrroleBXs and IndoleBXs.

In this section, only the synthesis of non-commercially available indole compounds is reported. The synthesis of the precursors for HeterocyclicBX reagents **11**, **16**, **17**, **21**, **23**, **26-48** had been already described by our group before. The procedures reported here are taken from the cited publications to facilitate reproduction of the results by having all the data in the same file.^[8,9]

2-(1-Methoxypent-3-yn-1-yl)-1-methyl-1H-pyrrole (**105**)

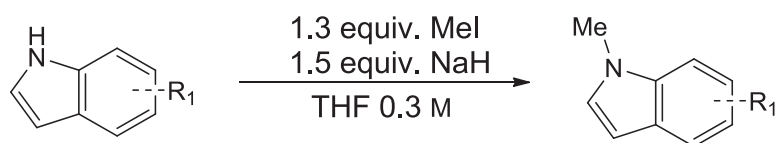


A 50 mL two-necked flask was charged with Mg (321 mg, 13.2 mmol, 1.32 equiv), HgCl₂ (2.7 mg, 0.10 mmol, 0.01 equiv) and dry diethyl ether (30 mL), then propargyl bromide was added dropwise (2.86 g, 12.0 mmol, 1.20 equiv). When the solution became homogeneous, **103** (1.09 g, 10.0 mmol, 1.00 equiv) was added dropwise. The reaction was quenched with sat NH₄Cl solution (30 mL) when TLC (Pentane/EtOAc: 5/1) indicated that the aldehyde was completely consumed after 4 hours. The aqueous and organic layers were separated; the aqueous layer was extracted with diethyl ether (3×20 mL). The combined organic layers were dried over MgSO₄ and concentrated under vacuum to obtain 1.34 g crude product as brown oil. The crude product was used for the next step directly without further purification. Crude propargylic alcohol (1.34 g, 8.98 mmol, 0.89 equiv) in THF (18 mL) was added into a suspension of NaH (237 mg, 9.88 mmol, 0.98 equiv) in THF (18 mL). 15 minutes later, MeI (1.40 g, 9.88 mmol, 1.10 equiv) was added into the mixture. The reaction was quenched with sat NH₄Cl after 4 h. The aqueous and organic layers were separated and the aqueous layer was extracted with ether (3×10 mL). After drying over MgSO₄, filtrating and concentrating under vacuum, the crude product was purified by column chromatography (Pentane:EtOAc= 15:1, 1 % Et₃N) to afford **104** as brown oil (1.00 g, 6.13 mmol, 61 % over two

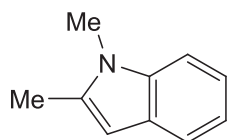
steps). Rf : 0.6 (Pentane:EtOAc 25:1). **¹H NMR** (400 MHz, CDCl₃) δ 6.62 (m, 1 H, ArH), 6.18 (dd, 1 H, J = 3.6, 1.8 Hz, ArH), 6.10 (dd, 1 H, J = 3.6, 2.7 Hz, ArH), 4.58 (t, 1 H, J = 6.9 Hz, CHO), 3.68 (s, 3 H, NCH₃), 3.27 (s, 3 H, OCH₃), 2.79 (ddd, 2 H, J = 16.8, 6.5, 2.7 Hz, CH₂), 2.05 (t, 1 H, J = 2.7 Hz, CH). **¹³C NMR** (101 MHz, CDCl₃) δ 129.9, 123.3, 108.5, 106.4, 80.7, 73.9, 69.8, 54.7, 34.0, 24.0.

448 mg of crude **104** (3.00 mmol), NaH (144 mg, 6.00 mmol, 2 equiv) and CH₃I (1.06 g, 7.50 mmol, 2.5 equiv) were used for the methylation with the same method as before. **105** was obtained as yellow oil (384 mg, 1.83 mmol, 48% over two steps). Rf: 0.5 (Pentane:EtOAc = 15:1). **¹H NMR** (400 MHz, CDCl₃) δ 6.59 (m, 1 H, ArH), 6.15 (dd, 1 H, J = 3.6, 1.8 Hz, ArH), 6.08 (dd, 1 H, J = 3.6, 2.7 Hz, ArH), 4.50 (m, 1 H, CHOCH₃), 3.66 (s, 3 H, NCH₃), 3.25 (s, 3 H, OCH₃), 2.72 (m, 2 H, CH₂), 1.79 (t, 3 H, J = 2.6 Hz, CH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 130.4, 123.1, 108.2, 106.4, 76.9, 75.4, 74.4, 54.6, 33.9, 24.3, 3.3.

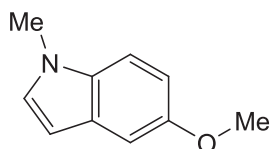
General Procedure GP1 for the N-Methylation of Indoles.



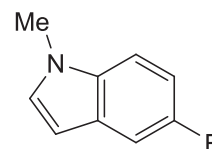
The corresponding indole (1.00 - 5.00 mmol, 1.00 equiv.) was dissolved in dry THF (0.3 M). Sodium hydride (60% suspension in mineral oil; 1.50 equiv.) was slowly added under N₂ flow at 0 °C. After being stirred at 0 °C for 15 min, the reaction mixture was allowed to warm to r.t for 1.5 h. It was then cooled back to 0 °C and methyl iodide (1.30 equiv.) was added. The mixture was warmed to r.t. and stirred overnight. After cooling again to 0° C, the reaction was quenched with water (10 mL), extracted with Et₂O (3 x 10 mL), the combined organic layers were dried over MgSO₄, and the solvent removed under reduced pressure. The resulting crude product was purified via flash column chromatography (Pentane:EtOAc 9:1-4:1), to give the desired N-methylated indole.



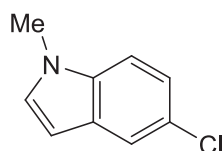
106



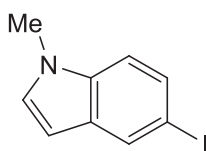
107



108

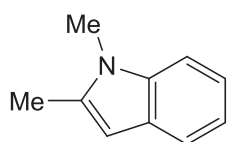


109



110

1,2-Dimethyl-1H-indole (106)



106

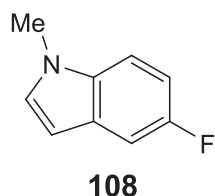
Starting from commercially available 2-methylindole (656 mg, 5.00 mmol), 1,2-dimethyl-1H-indole **106** (683 mg, 4.70 mmol, 94% yield) was obtained as an off-white solid. **IR** ν (neat) 3050 (w), 3020 (w), 2970 (m), 1610 (w), 1400 (s), 1340 (m), 1240 (m), 930 (m), 910 (w), 780 (m), 750 (m), 730 (s). **¹H NMR** (400 MHz CDCl₃) δ 7.69 (d, J = 7.8 Hz, 1H, ArH), 7.41 (dd, J = 8.1, 1.0 Hz, ArH), 7.32 (m, 1H, ArH), 7.24 (ddd, J = 8.0, 7.0, 1.1 Hz, 1H, ArH), 6.42 (s, 1H, NC(CH₃)CH), 3.79 (s, 3H, NCH₃), 2.57 (d, J = 1.0 Hz, 3H, NCCH₃). **¹³C NMR** (125 MHz, CDCl₃) δ 138.1, 136.9, 128.1, 120.6, 119.8, 119.4, 108.8, 99.7, 29.5, 12.9. ¹H NMR values are in accordance with the data reported in literature.^[10]

5-Methoxy-1-methyl-1H-indole (107)

Starting from commercially available 5-methoxy-1H-indole (736 mg, 5.00 mmol), 5-methoxy-1-methyl-1H-indole **107** (730 mg, 4.53 mmol, 91% yield) was obtained as a colorless crystalline solid. **IR** ν 2952 (w), 2918 (w), 2834 (w), 1622 (m), 1608 (w), 1577 (w), 1496 (s), 1459 (w), 1450 (m), 1449 (m), 1421 (s), 1347 (w), 1293 (w), 1243 (s), 1191 (m), 1152 (s), 1102 (w), 1026 (m), 942 (w), 855 (m), 845 (w), 805 (s). **¹H NMR** (400 MHz, CDCl₃) δ 7.30 (d, 1H, J = 8.5 Hz, ArH) 7.13 (s, 1H, ArH),

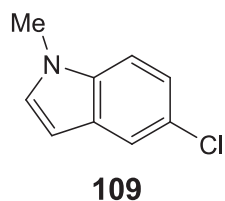
7.05 (s, 1 H, ArH), 6.92 (d, 1H, $J = 8.8$ Hz, ArH), 6.43 (d, 1H, $J = 1.0$ Hz, ArH), 3.90 (s, 3H, NMe), 3.80 (s, 3H, OMe). ^{13}C NMR (101 MHz, CDCl_3) δ 154.0, 132.2, 129.3, 128.8, 111.9, 109.9, 102.5, 100.4, 55.9, 33.0.

5-Fluoro-1-methyl-1H-indole (108)



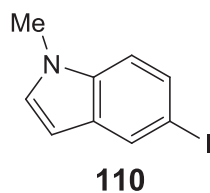
Starting from commercially available 5-fluoro-1H-indole (676 mg, 5.00 mmol), 5-fluoro-1-methyl-1H-indole **108** (683 mg, 4.58 mmol, 92% yield) was obtained as a colorless solid. IR 3104 (w), 2946 (w), 2922 (w), 2907 (w), 2887 (w), 2362 (w), 2343 (w), 1626 (w), 1576 (w), 1514 (m), 1492 (s), 1449 (m), 1423 (m), 1340 (m), 1283 (m), 1238 (s), 1228 (s), 1140 (m), 1129 (m), 1122 (m), 1100 (m), 1081 (m), 1013 (w), 949 (m), 859 (m), 811 (s). ^1H NMR (400 MHz, CDCl_3) δ 7.31 (dd, $J = 9.7, 2.4$ Hz, 1H, ArH), 7.26 (m, 1H, ArH), 7.12 (d, $J = 3.1$ Hz, 1H, ArH), 7.01 (dt, $J = 9.1, 2$ Hz, 1H, ArH), 6.48 (dd, $J = 3.1, 0.7$ Hz, 1H, ArH). 3.81 (s, 3H, NCH₃). ^{13}C NMR (101 MHz, CDCl_3) δ 158.0 (d, $J\text{-F}_6 = 232$ Hz), 133.4, 130.4, 128.7 (d, $J\text{-F}_6 = 10$ Hz), 109.9 (d, $J\text{-F}_6 = 15$ Hz), 109.8, 105.5 (d, $J\text{-F}_6 = 23$ Hz), 100.8 (d, $J\text{-F}_6 = 5.0$ Hz), 33.1.

5-Chloro-1-methyl-1H-indole (109)



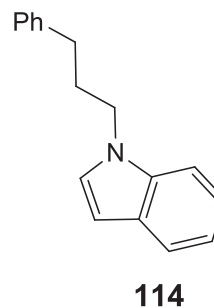
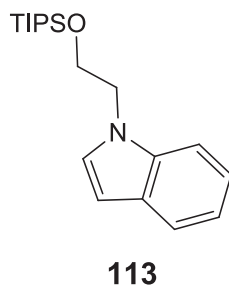
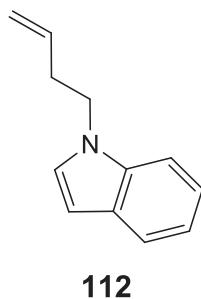
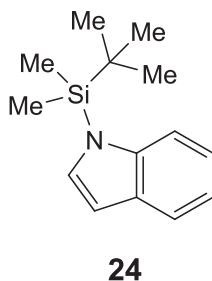
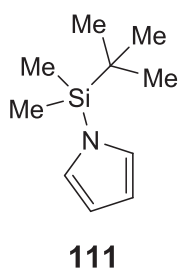
Starting from commercially available 5-chloro-1H-indole (758 mg, 5.00 mmol), 5-chloro-1-methyl-1H-indole **109** (800 mg, 4.83 mmol, 97% yield) was obtained as a colorless solid. IR ν 3102 (w), 2943 (w), 2913 (w), 2881 (w), 2817 (w), 1567 (w), 1513 (m), 1475 (s), 1441 (m), 1421 (s), 1379 (w), 1331 (m), 1278 (s), 1241 (s), 1199 (m), 1146 (m), 1106 (w), 1082 (m), 1063 (s), 1009 (m), 909 (m), 870 (m), 869 (m). ^1H NMR (400 MHz, CDCl_3) δ 7.64 (d, $J = 2.1$ Hz, 1H, ArH), 7.30 – 7.19 (m, 2H, ArH), 7.10 (d, $J = 3.1$ Hz, 1H, ArH), 6.47 (dd, $J = 3.1, 0.7$ Hz, 1H, ArH), 3.80 (s, 3H, NCH₃). ^{13}C NMR (101 MHz, CDCl_3) δ 135.1, 130.1, 130.1, 125.1, 121.8, 120.2, 110.2, 100.6, 33.1.

5-Iodo-1H-indole (110)

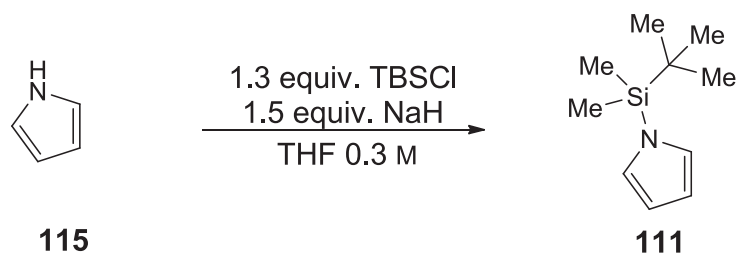


Starting from commercially available 5-iodo-1*H*-indole (257 mg, 1.00 mmol), 5-iodo-1-methyl-1*H*-indole **110** (380 mg, 0.755 mmol, 76% yield) was obtained as a colorless solid. **IR** ν 3093 (w), 3053 (w), 2940 (w), 2919 (w), 2886 (w), 2876 (w), 2856 (w), 1557 (m), 1510 (s), 1473 (s), 1432 (m), 1420 (s), 1379 (w), 1329 (m), 1277 (s), 1242 (s), 1193 (w), 1151 (w), 1103 (m), 1079 (m), 1045 (w), 1007 (m), 888 (s), 868 (m). **¹H NMR** (400 MHz, CDCl₃) δ 7.98 (s, 1 H, Ar*H*), 7.49 (d, J = 8.6 Hz, 1H, Ar*H*), 7.13 (d, J = 8.6 Hz, 1H, Ar*H*), 7.04 (s, 1H, Ar*H*), 6.43 (s, 1H, Ar*H*), 3.80 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 135.8, 131.0, 129.8, 129.7, 129.6, 111.3, 100.3, 82.9, 33.0.

N-Functionalized Indoles

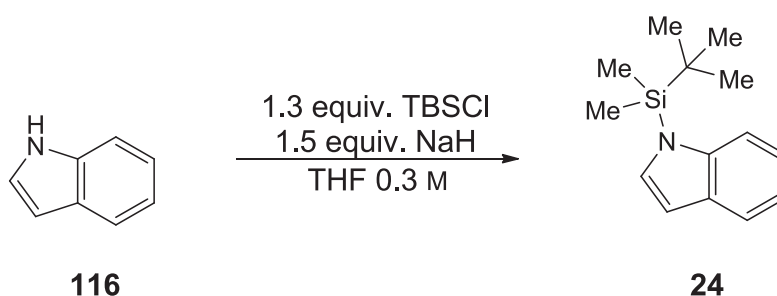


1-(1-(*tert*-Butyldimethylsilyl)-1*H*-pyrrole (111)



Following a reported procedure,^[5] commercially available 1*H*-pyrrole **115** (700 μ l, 10.0 mmol) was dissolved in dry THF (30 ml, 0.3 M). Sodium hydride (60% suspension in mineral oil; 600 mg, 15.0 mmol, 1.50 equiv.) was slowly added under N₂ flow at 0 °C. After being stirred at 0°C for 15 min, the reaction mixture was allowed to warm to r.t for 1.50 h. Then it was cooled back to 0°C and *tert*-butylchlorodimethylsilane (1.96 g, 13.0 mmol, 1.30 equiv.) was added. The mixture was warmed to r.t. and stirred overnight. The reaction was quenched by addition of water (10 mL) at 0°C. The aqueous layer was extracted with Et₂O (3 x 10 mL), the combined organic layers were dried over MgSO₄, and the solvent was removed under reduced pressure. The crude product was purified via flash column chromatography (Pentane:EtOAc 8:1), to give the desired 1-(*tert*-butyldimethylsilyl)-1*H*-pyrrole **111** (1.30 g, 7.17 mmol, 72% yield). IR ν 3100 (w), 2956 (m), 2931 (m), 2858 (m), 1707 (w), 1473 (m), 1364 (w), 1259 (s), 1222 (w), 1190 (s), 1084 (s), 1048 (s), 1008 (w), 942 (w), 839 (s). ¹H NMR (400 MHz, CDCl₃) δ 6.86 – 6.62 (m, 2H, Ar*H*), 6.39 – 6.21 (m, 2H, Ar*H*), 0.86 (s, 9H, SiC(CH₃)₃), 0.41 (s, 6H, Si(CH₃)₂). ¹H NMR values are in accordance with the data reported in literature.^[11]

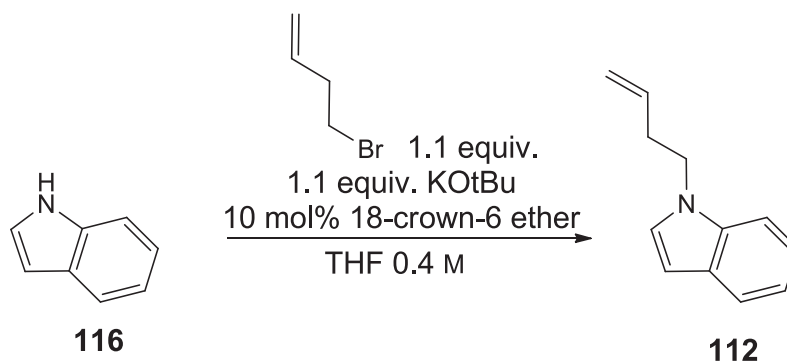
1-(*tert*-Butyldimethylsilyl)-1*H*-Indole (**24**)



Following a reported procedure,^[12] commercially available 1*H*-indole **34** (586 mg, 5.00 mmol) was dissolved in dry THF (10 mL, 0.5 M). Sodium hydride (60% suspension in mineral oil; 300 mg, 7.50 mmol, 1.50 equiv.) was slowly added under N₂ atmosphere at 0 °C. After being stirred at 0

°C for 15 min, the reaction mixture was allowed to warm to r.t for 1.5 h. Then it was cooled back to 0 °C and *tert*-butylchlorodimethylsilane (980 mg, 6.50 mmol, 1.30 equiv.) was added. The mixture was warmed to r.t. and stirred overnight. After cooling again to 0 °C, the reaction was quenched with water (10 mL), extracted with Et₂O (3 x 10 mL), the combined organic layers were dried over MgSO₄, and the solvent was removed under reduced pressure. The residue was purified via flash column chromatography (Pentane:EtOAc 4:1), to give the desired 1-(*tert*-butyldimethylsilyl)-1*H*-indole **24** (869 mg, 3.76 mmol, 75% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.79 (m, 1H, Ar*H*), 7.72 (dt, *J* = 8.2, 1.1 Hz, 1H, Ar*H*), 7.37 (d, *J* = 3.2 Hz, 1H, Ar*H*), 7.32 (ddd, *J* = 8.3, 7.0, 1.6 Hz, 1H, Ar*H*), 7.25 (m, 1H), 6.78 (dd, *J* = 3.3, 1.0 Hz, 1H, Ar*H*), 1.11 (s, 9H, SiCCH₃), 0.78 (s, 6H, Si(CH₃)₂). IR ν 3064.6 (w), 2950.5 (w), 2929.7 (m), 2855.9 (w), 1512.0 (s), 1427.6 (s), 1449.9 (m), 1284.3 (s), 1271.6 (s), 1255.8 (m), 1158.9 (s), 1140.9 (s), 984.2 (w), 840.1 (m). ¹H NMR values are in accordance with the data reported in literature.^[13]

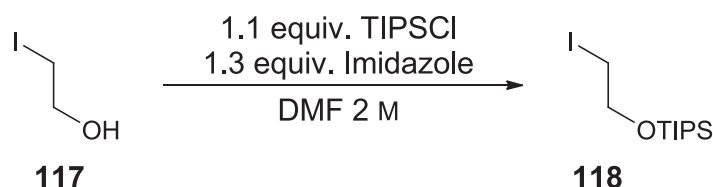
1-(But-3-en-1-yl)-1*H*-Indole (**112**)



Following a reported procedure,^[14] potassium *tert*butoxide (1.24 mg, 11.0 mmol, 1.10 equiv.) was added to a solution of 18-crown-6 ether (26.4 mg, 0.100 mmol, 10 mol%) in dry THF (25 mL, 0.4 M) under a nitrogen atmosphere. Then, commercially available 1*H*-indole **116** (1.17 g, 10.0 mmol, 1.00 equiv.) was added under vigorous stirring. The reaction was cooled to 0°C in an ice bath. A solution of 4-bromobut-1-ene (1.20 mL, 11.0 mmol, 1.10 equiv.) in THF (5 mL) was added dropwise to the reaction mixture and the latter was stirred overnight. After cooling again to 0 °C, the reaction was quenched with water (20 mL), extracted with Et₂O (3 x 20 mL), the combined organic layers were dried over MgSO₄, and the solvent was removed under reduced pressure. The

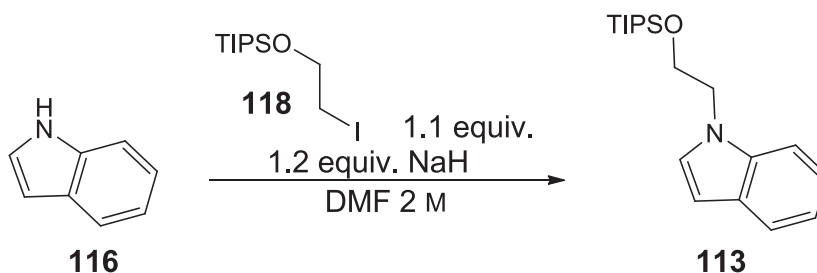
residue was purified via flash column chromatography (Pentane:EtOAc 9:1) to give the desired 1-(but-3-en-1-yl)-1*H*-indole **112** (280 mg, 1.64 mmol, 17% yield) as a yellow oil. **IR** ν 2936 (w), 1640 (s), 1612 (s), 1508 (m), 1458 (s), 910 (m), 740 (m), 712 (m). **¹H NMR** (400 MHz, CDCl₃) δ 7.84 (d, J = 8.0 Hz, 1H, Ar*H*), 7.52 (d, J = 8.2 Hz, 1H, Ar*H*), 7.41 (t, J = 7.6 Hz, 1H, Ar*H*), 7.31 (t, J = 7.4 Hz, 1H, Ar*H*), 7.23 (d, J = 3.2 Hz, 1H, Ar*H*), 6.68 (d, J = 3.2 Hz, 1H, Ar*H*), 5.94 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H, Ar*H*), 5.32 – 5.12 (m, 2H, NCH₂CH₂CH=CH₂), 4.31 – 4.27 (m, 2H, CH₂), 2.72 (q, J = 7.1 Hz, 2H, CH₂). **¹H NMR** values are in accordance with the data reported in literature.^[15]

(2-Iodoethoxy)triisopropylsilane (**118**)



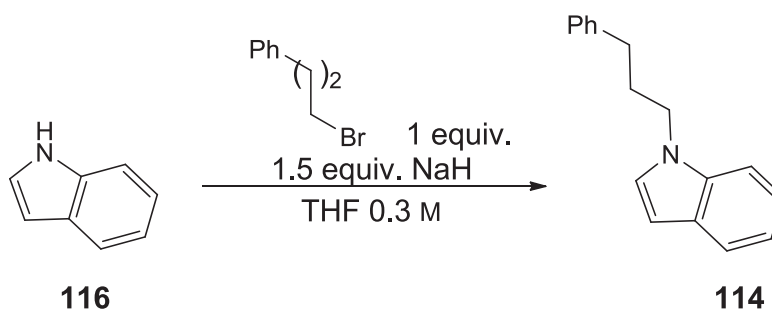
Following a reported procedure,^[16] commercially available 2-iodoethanol **117** (1.10 mL, 10.0 mmol, 1.00 equiv.) was added to a solution of imidazole (885 mg, 13.0 mmol, 1.30 equiv.) in DMF (5 mL, 2.0 M) under nitrogen atmosphere. chloro-triisopropylsilane (2.80 mL, 13.0 mmol, 1.30 equiv.) was then added dropwise. After 1 h, the reaction turned into a thick suspension and a colorless solid precipitated. The mixture was allowed to warm to room temperature removed and was stirred for an additional hour. Water (5 mL) was added to dissolve the solid. The organic layer was separated and eluted through a SiO₂ plug with pentane (100 mL). The solvent was removed under reduced pressure to give (2-iodoethoxy)triisopropylsilane **118** (3.15 g, 9.60 mmol, 96% yield) as a slightly yellow oil. **IR** ν 2958 (m), 2942 (m), 2891 (w), 2866 (m), 1464 (m), 1384 (w), 1275 (w), 1249 (w), 1190 (w), 1169 (w), 1123 (s), 1092 (s), 1069 (s), 1013 (w), 999 (m), 943 (w), 920 (w), 882 (s), 857 (w). **¹H NMR** (400 MHz, CDCl₃) δ 3.85 (t, J = 6.9 Hz, 2H, OCH₂), 3.15 (t, J = 7.0 Hz, 2H, ICH₂), 1.11-0.88 (m, 21H, TIPS). **¹³C NMR** (101 MHz, CDCl₃) δ 64.6, 18.0, 12.1, 6.9.

1-(2-((Triisopropylsilyl)oxy)ethyl)-1*H*-Indole (**113**)



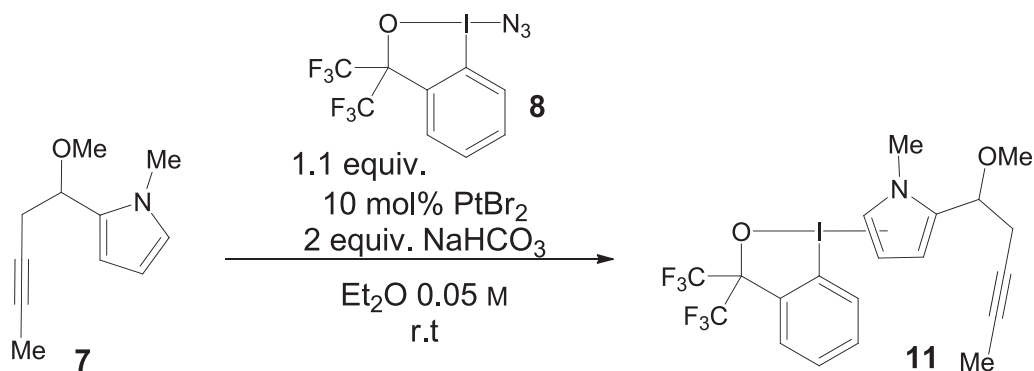
Commercially available 1*H*-indole **116** (586 mg, 5.00 mmol) was dissolved in *N,N*-dimethylformamide (5 mL, 0.5 M *in total*). Sodium hydride (60% suspension in mineral oil; 144 mg, 6.00 mmol, 1.20 equiv.) was added at r.t. and the reaction mixture was stirred for one hour. *N,N*-Dimethylformamide (5 mL) was then added to dissolve the resulting colorless precipitate. The reaction was cooled to 0 °C and (2-iodoethoxy)triisopropylsilane **118** (1.90 g, 5.50 mmol, 1.10 equiv.) was added dropwise. The reaction mixture was stirred overnight, allowing it to warm to r.t. The reaction was then quenched with water (20 mL) and the reaction mixture was extracted with EtOAc (3 x 25 mL). The combined organic layers were washed with water (10 mL), brine (3x10 mL), and dried over MgSO₄. The solvent was then removed under reduced pressure. Flash column chromatography (Pentane:EtOAc 9:1) afforded 1-(2-((triisopropylsilyl)oxy)ethyl)- 1*H*-indole **113** (1.20 g, 3.78 mmol, 76% yield) as a colorless oil. IR ν 3056 (w), 2891 (m), 2865 (s), 1514 (w), 1464 (s), 1439 (w), 1387 (w), 1360 (w), 1334 (w), 1317 (m), 1115 (s), 1077 (m), 1013 (m), 923 (m), 819 (w). ¹H NMR (400 MHz, CDCl₃) δ 7.66 (m, 1 H, Ar*H*), 7.38 (dd, *J* = 8.2, 0.8 Hz, 1H, Ar*H*), 7.25 - 7.19 (m, 2H, Ar*H*), 7.13 (m, 1H, Ar*H*), 6.52 (dd, *J* = 3.1, 0.8 Hz, 1H, Ar*H*), 4.30 (t, *J* = 6.0 Hz, 2H, CH₂), 4.04 (t, *J* = 5.8 Hz, 2H, CH₂), 1.17 - 0.85 (m, 21H, TIPS). ¹³C NMR (101 MHz, CDCl₃) δ 136.1, 128.7, 128.6, 121.3, 120.9, 119.2, 109.3, 101.0, 62.8, 48.8, 17.9, 11.9.

1-(3-Phenylpropyl)-1*H*-indole (114)



Following a reported procedure,^[17] commercially available 1*H*-indole **116** (585 mg, 5.00 mmol, 1.00 equiv.) was dissolved in THF (15 mL). Sodium hydride (60% suspension in mineral oil; 300 mg, 7.50 mmol, 1.50 equiv.) was added at 0 °C and the reaction mixture was stirred for 30 min. (3-bromopropyl)benzene (760 μ L, 5.00 mmol, 1.00 equiv.) was then added dropwise. After 15 min the ice bath was removed and the reaction mixture was stirred for 4 hours at r.t.. The reaction was cooled back to 0 °C, quenched with water, diluted with EtOAc (10 mL), extracted with water (2 x 10 mL), washed with brine (10 mL), and dried over MgSO₄. After filtration, the solvent was removed under reduced pressure. Flash column chromatography (Pentane:EtOAc 20:1) afforded 1-(3-phenylpropyl)-1*H*-indole **114** (1.12 g, 4.76 mmol, 95% yield) as a colorless oil. **IR** 3085 (w), 3057 (w), 3026 (w), 3004 (w), 2946 (w), 2945 (w), 2870 (w), 1780 (w), 1738 (s), 1717 (s), 1612 (w), 1603 (w), 1511 (m), 1497 (m), 1483 (m), 1464 (s), 1455 (s), 1400 (m), 1377 (s), 1354 (s), 1336 (s), 1315 (s), 1254 (s), 1207 (s), 1179 (m), 1166 (m), 1143 (m), 1143 (m), 1122 (m), 1114 (m), 1080 (m), 1031 (m), 1020 (m), 1004 (w), 952 (w), 928 (w), 909 (w), 885 (m), 855 (w), 838 (w), 821 (w), 811 (w), 802 (w). **¹H NMR** (400 MHz, CDCl₃) δ 7.87 (d, *J* = 8 Hz, 1H, Ar*H*), 7.53-7.23 (m, 9H, Ar*H*), 6.72 (dd, *J* = 3.1, 0.8 Hz, 1H, Ar*H*), 4.26 (t, *J* = 7.1 Hz, 2H, NCH₂), 2.77 (t, *J* = 8 Hz, 2H, CH₂Ph), 2.34 (qi, *J* = 7.8 Hz, 2H, CH₂CH₂CH₂). **¹³C NMR** (101 MHz, CDCl₃) δ 141.2, 136.2, 128.7, 128.7, 128.6, 128.0, 126.3, 121.6, 121.2, 119.5, 109.6, 101.3, 45.8, 33.2, 31.7 (*one aromatic Carbon signal not resolved*).

2.3 Synthesis of compound 10/11.



A solution of 2-(1-methoxypent-3-yn-1-yl)-1-methyl-1*H*-pyrrole **7** (0.100 mmol, 1.0 equiv) in THF (0.33 mL) was added into a solution of PtBr₂ (3.55 mg, 10.0 μ mol, 0.10 equiv), NaHCO₃ (17.0 mg, 0.200 mmol, 2.0 equiv) and 1-azido-3,3-bis(trifluoromethyl)-3-(1*H*)-1,2-benziodoxole **8** (330 mg, 0.600 mmol, 2.00 equiv) in CH₃CN (0.180 mL). The reaction was stopped after 72 hrs, EtOAc was

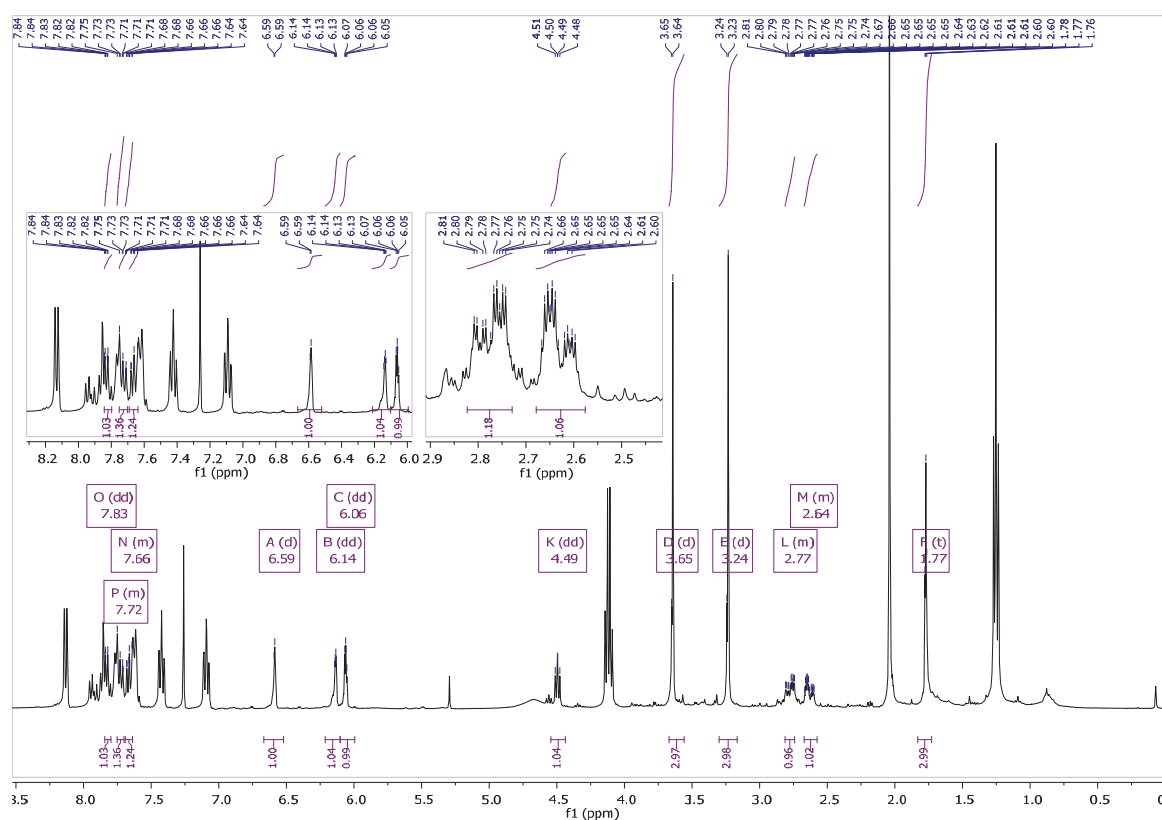
added to solubilize the precipitate and a TLC (Pentane:EtOAc 4:1 for the starting, DCM:MeOH 9:1 for the product) was taken: full conversion of the starting to **11**. The solvent was removed under reduced pressure, and a crude NMR (extremely wet of EtOAc) and a MS analysis were taken.

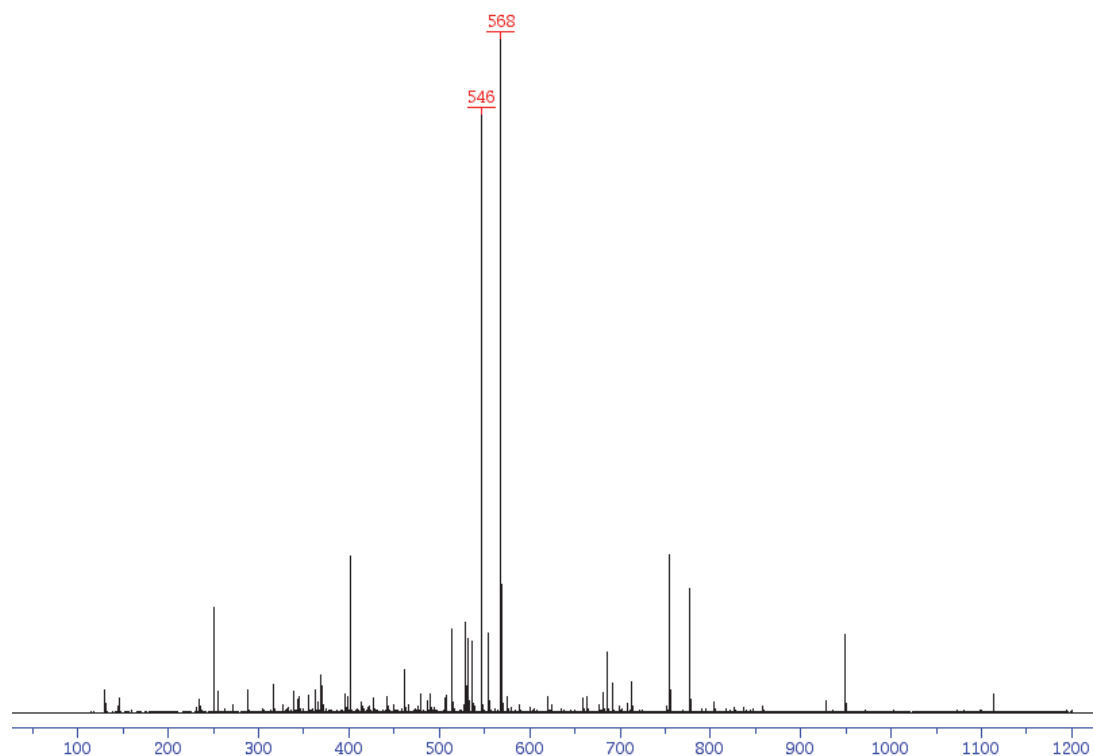
HR-ESI-MS 546.0372 ($[M+H]^+$, $C_{20}H_{18}F_6INO_2^+$; calc. for 545.02864)

The crude 1H -NMR shows a 2:1 ratio between known peaks of iodobenzoic hexafluorodimethyl-alcohol and the new product. The peak of the new compound are reported here:

1H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, $J = 6.8, 1.4$ Hz, 1H, *ArH*), 7.75 – 7.70 (m, 1H, *ArH*), 7.69 – 7.64 (m, 1H, *ArH*), 6.59 (d, $J = 2.2$ Hz, 1H, *ArH*), 6.14 (dd, $J = 3.6, 1.8$ Hz, 1H, *ArH*), 6.06 (dd, $J = 3.6, 2.7$ Hz, 1H, *ArH*), 4.49 (dd, $J = 7.5, 6.3$ Hz, 1H, *CH*), 3.65 (m, 3H, *CH*₃), 3.24 (m, 3H, *CH*₃), 2.77 (m, 1H, *CH*₂), 2.64 (m, 1H, *CH*₂), 1.77 (t, $J = 2.5$ Hz, 3H, *CH*₃).

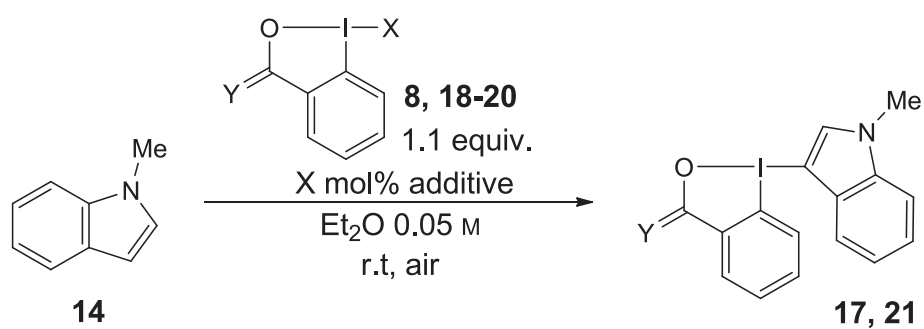
Subsequently, the crude was columned over silica using an eluent mixture of 9:1 DCM:MeOH; no product was obtained as the compound degraded on silica.





2.4 Optimization in the synthesis of IndoleBX 21.

Table S1: Screening of additives



Entry	Y	X	Additive (mol%)	Yield% ^a
1	(CF ₃) ₂	N ₃ (8)	-	25%
2	(CF ₃) ₂	OAc (18)	-	-
3	(CF ₃) ₂	OAc (18)	Zn(OTf) ₂ (10)	56%
4	O	OH (19)	TMSOTf (10)	— ^b
5	O	OH (19)	Zn(OTf) ₂ (10)	— ^b

6	O	OAc (20)	-	– ^b
7	O	OAc (20)	TMSOTf (10)	16%
8	O	OAc (20)	Zn(OTf)₂ (10)	36%^b
9	O	OAc (20)	Cu(OTf) ₂ (10)	36% ^c
10	O	OAc (20)	AgNTf ₂ (20)	– ^c
11	O	OAc (20)	AgF (20)	– ^c
12	O	OAc (20)	CsF (20)	– ^c
13	O	OAc (20)	TBAF (20)	– ^c

a) Substrate **14** (0.100 mmol), **reagents 8, 18-20** (0.110 mmol), **additive** (X mol%), and Et₂O (0.05 M) at 25 °C. Isolated yield after flash chromatography is given. b) No conversion: starting materials recovered. c) Complete decomposition of the hypervalent iodine reagents.

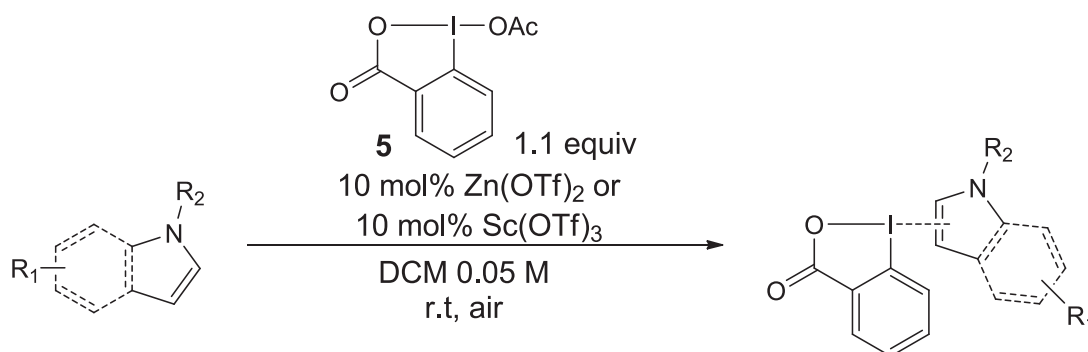
Table S2: Screening of solvents and additive loading

Entry	Solvent	X mol% Zn(OTf) ₂	Yield% ^a
1	THF	10	– ^b
2	THF	20	– ^b
3	THF	1 equiv.	– ^b
4	DCM	10	Full conversion ^c
5	DCM	20	97%
6	DCM	1 equiv.	decomposition

a) Substrate **14** (0.100 mmol), AcOBX **20** (0.110 mmol), Zn(OTf)₂ (x mol%), and **solvent** (0.05 M) at 25 °C. Isolated yield after flash chromatography is given. b) No conversion: starting materials recovered. c) 2 equiv. of OAcBX **20** are needed.

2.5 Preparation of PyrroleBX and IndoleBX Reagents.

General Procedure GP2 for the Synthesis of Heterocyclic-BX Reagents 17, 21, 23, 25-47, 49



Note: prior to the reaction, the glassware requires to be carefully cleaned with aqua regia to remove all metal traces; the commercially available heterocyclic starting material were purified through a short plug of silica prior to being used.

Procedure A for 1.00 mmol: in an open air flask, the corresponding heterocycle (1.00 mmol, 1.00 equiv.), freshly prepared Acetoxy-benziodoxole **20** (1.10 mmol, 1.10 equiv.) and Zinc(II) trifluoromethanesulfonate (72.7 mg, 0.200 mmol, 20 mol%) were dissolved in DCM (20 mL 0.05 M). The reaction was stirred while being monitored by TLC (Pentane:EtOAc 9:1 for the starting materials, DCM:MeOH 9:1 for the products). Upon consumption of the starting material, the crude was directly submitted to short-path flash chromatography (DCM:MeOH 10:1 or EtOAc:MeOH 10:1 for the separation of pyrrole-based reagents) to afford the desired Heterocyclic-BX compounds **17, 21, 23, 25-37, 43-48**.

Procedure B for 0.200 mmol: in an open air flask, the corresponding heterocycle (0.200 mmol, 1.00 equiv.), freshly prepared Acetoxy-benziodoxoles **17, 23, 95-97** (0.220 mmol, 1.10 equiv.) and zinc(II) trifluoromethanesulfonate (7.27 mg, 0.040 mmol, 20 mol%) were dissolved in DCM (4 mL 0.05 M). The reaction was stirred while being monitored by TLC (Pentane:EtOAc 9:1 for the starting materials, DCM:MeOH 9:1 for the products). Upon consumption of the starting material, the crude was directly submitted to short-path flash chromatography (DCM:MeOH 10:1 or EtOAc:MeOH 10:1 for the separation of pyrrole-based reagents) to afford the desired Heterocyclic-BX compounds **32-43**.

The structure of compounds 25 and 34 was confirmed by X-Ray analysis (see par. 5 of the Supplementary Informations).

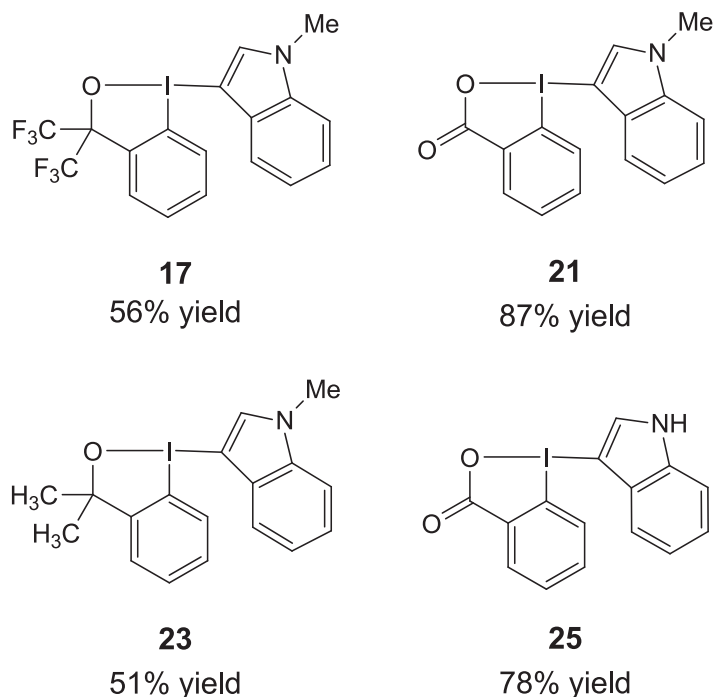
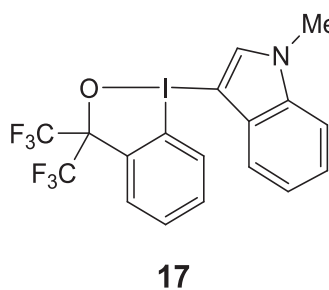


Figure S1: Scope of Heterocyclic-BX reagents (1)

1-(3-(1-Methyl-1*H*-indole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ₃-benzo[*d*][1,2]iodaoxole (17)

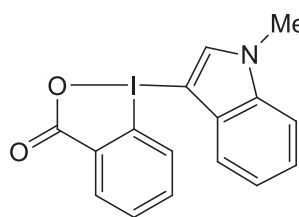


Following procedure **B**: starting from commercially available 1-methyl-1-*H*-indole **14** (26.2 mg, 0.100 mmol), 1-acetoxy-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole **18** (94.0 mg, 0.220 mmol, 1.10 equiv.) and in Et₂O 0.05 M, after 16 hours 1-(3-(1-methyl-1*H*-indole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ³-benzo[*d*][1,2]iodaoxole **17** (56.1 mg, 0.112 mmol, 56% yield) was

obtained as a brown foam. **Rf**: 0.7 (DCM:MeOH 9:1). **IR** ν 3069 (w), 2922 (w), 2852 (w), 1732 (w), 1504 (m), 1457 (w), 1263 (s), 1212 (m), 1178 (s), 1157 (s), 1130 (m), 1047 (w), 948 (s). **¹H NMR** (400 MHz, CDCl₃) δ 7.86 (m, 1H, Ar*H*), 7.53 (s, 1H, NCHCl), 7.52 – 7.46 (m, 3H, Ar*H*), 7.41 (ddd, *J* = 8.3, 7.0, 1.1 Hz, 1H, Ar*H*), 7.28 (m, 1H, Ar*H*), 7.23 (m, 1H, Ar*H*), 6.95 (d, *J* = 8.3 Hz, 1H, Ar*H*), 3.96 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 137.5, 137.4, 131.7, 131.4, 130.1, 129.9, 126.9, 123.9, 123.2 (m), 122.1, 120.4, 112.2, 110.3, 84.2, 81.55 (dt, *J* = 57.1, 28.5 Hz), 33.6 (one aromatic Carbon signal not resolved). **HR-ESI-MS** 499.9946 ([M+H]⁺,

$C_{18}H_{13}F_6INO^+$; calc. for 499.9941). The structure of the obtained regioisomer was assigned by NMR analysis.^[18]

1-(3-1-Methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (21)

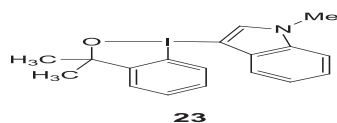


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The synthesis of 1-(3-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **21** was scaled up to 10 mmol without reoptimization of the protocol.

Following procedure **A**: starting from commercially available 1-methyl-1-*H*-indole **14** (1.35 g, 10.0 mmol), after 16 hours 1-(3-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **21** (3.28 g, 8.70 mmol, 87% yield) was obtained as a brown foam. **Rf**: 0.4 (DCM:MeOH 9:1). **IR** ν 3107 (w), 3059 (w), 2948 (w), 1599 (s), 1552 (m), 1506 (m), 1454 (w), 1392 (m), 1277 (s), 1245 (s), 1225 (s), 1166 (s), 1131 (m), 1031 (s), 1004 (w), 842 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.40 (dd, J = 7.5, 1.7 Hz, 1H, Ar*H*), 7.82 (s, 1H, NCHCl), 7.55 – 7.48 (m, 2H, Ar*H*), 7.39 – 7.35 (m, 2H, Ar*H*), 7.34 – 7.23 (m, 2H, Ar*H* + CDCl₃), 6.84 (d, J = 8.3 Hz, 1H, Ar*H*), 4.02 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 166.8, 138.6, 137.6, 133.4, 133.3, 132.5, 130.5, 129.3, 125.2, 124.3, 122.6, 119.9, 116.1, 110.7, 78.9, 33.9. **HR-ESI-MS** 377.9990 ([*M*+*H*]⁺, C₁₆H₁₃INO₂⁺; calc. for 377.9986). The structure of the obtained regioisomer was assigned by NMR correlation to compound **25**. DSC-analysis was performed on compound **21**: see par.5 of Supplementary informations.

1-(3-1-Methyl-1*H*-indole)-3,3-dimethyl-1,3-dihydro-1λ³-benzo[*d*][1,2]iodoxole (23)

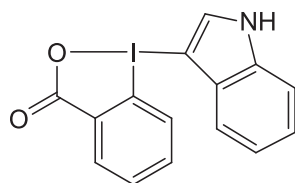


23

Following procedure **B**: starting from commercially available 1-methyl-1-*H*-indole **14** (26.2 mg, 0.100 mmol) and 3,3-dimethyl-1λ₃-benzo[*d*][1,2]iodoxol-1(3*H*)-yl acetate **22** (70.4 mg, 0.220 mmol, 1.10 equiv.), after 16 hours 1-(3-1-methyl-1*H*-indole)-3,3-dimethyl-1,3-dihydro-1λ³-benzo[*d*][1,2]iodoxole **23** (40.1 mg, 0.102 mmol, 51% yield) was obtained as a brown foam. **Rf**: 0.7 (DCM:MeOH 9:1). **IR** ν 3115 (w), 3050 (w), 2986 (w), 1509 (w), 1455 (w), 1372 (w), 1284 (s), 1247 (s), 1225 (m), 1166 (m), 1110 (w), 1031 (s), 992 (w). **¹H NMR** (400 MHz, CDCl₃) δ 7.92 (s, 1H, NCHCl), 7.54 (m, 1H, Ar*H*), 7.47 (m, 1H, Ar*H*), 7.45 – 7.40 (m, 3H, Ar*H*), 7.34 (ddd, J = 8.0, 6.9, 1.0 Hz, 1H,

ArH), 7.08 (ddd, $J = 8.7, 5.8, 2.9$ Hz, 1H, ArH), 6.87 (m, 1H, ArH), 4.02 (s, 3H, NCH₃), 1.75 (s, 6H, C(CH₃)₂). ¹³C NMR (101 MHz, CDCl₃) δ 146.3, 140.2, 137.7, 130.9, 130.4, 128.9, 128.7, 127.0, 124.8, 123.3, 119.6, 111.0, 108.9, 74.6, 72.9, 34.2, 30.5. **HR-ESI-MS** 392.0510 ([M+H]⁺, C₁₈H₁₉INO⁺; calc. for 392.0506). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 17.*

1-(3-1*H*-indole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one (25)



25

Following procedure **A**: starting from 1-(*tert*-butyldimethylsilyl)-1*H*-indole **24** (231 mg, 1.00 mmol) and using Sc(OTf)₃ as the Lewis acid (20 mol %), after 16 hours 1-(3-1*H*-indole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **25** (294 mg, 8.10 mmol, 78% yield) was obtained as a brown solid. **Rf**: 0.4 (DCM:MeOH 9:1). **Mp**: 174.2°C (decomposition). **IR** ν 3302 (w), 2975 (w), 2903 (w), 1722 (w), 1609 (m), 1584 (m), 1557 (w), 1490 (w), 1457 (w), 1385 (w), 1277 (s), 1258 (s), 1230 (m), 1174 (m), 1087 (w), 1036 (s), 880 (w), 841 (w). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.33 (s, 1H, NH), 8.21 (s, 1H, NCHCl), 8.08 (dd, $J = 7.3, 1.7$ Hz, 1H, ArH), 7.59 (d, $J = 8.2$ Hz, 1H, ArH), 7.52 (t, $J = 7.3$ Hz, 1H, ArH), 7.43 (d, $J = 7.5$ Hz, 1H, ArH), 7.36 (ddd, $J = 8.5, 7.3, 1.7$ Hz, 1H, ArH), 7.26 (ddd, $J = 8.2, 7.0, 1.2$ Hz, 1H, ArH), 7.15 (t, $J = 7.5$ Hz, 1H, ArH), 6.72 (d, $J = 8.5$ Hz, 1H, ArH). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 166.1, 136.6, 134.5, 133.3, 131.4, 130.2, 128.5, 126.3, 123.4, 122.3, 121.6, 119.2, 116.1, 112.9, 80.0. **HR-ESI-MS** 363.9832 ([M+H]⁺, C₁₅H₁₁INO₂⁺; calc. for 363.9829). *The structure of the reagent was determined through X-Ray diffraction of a single crystal (CCDC number: 1540821).*

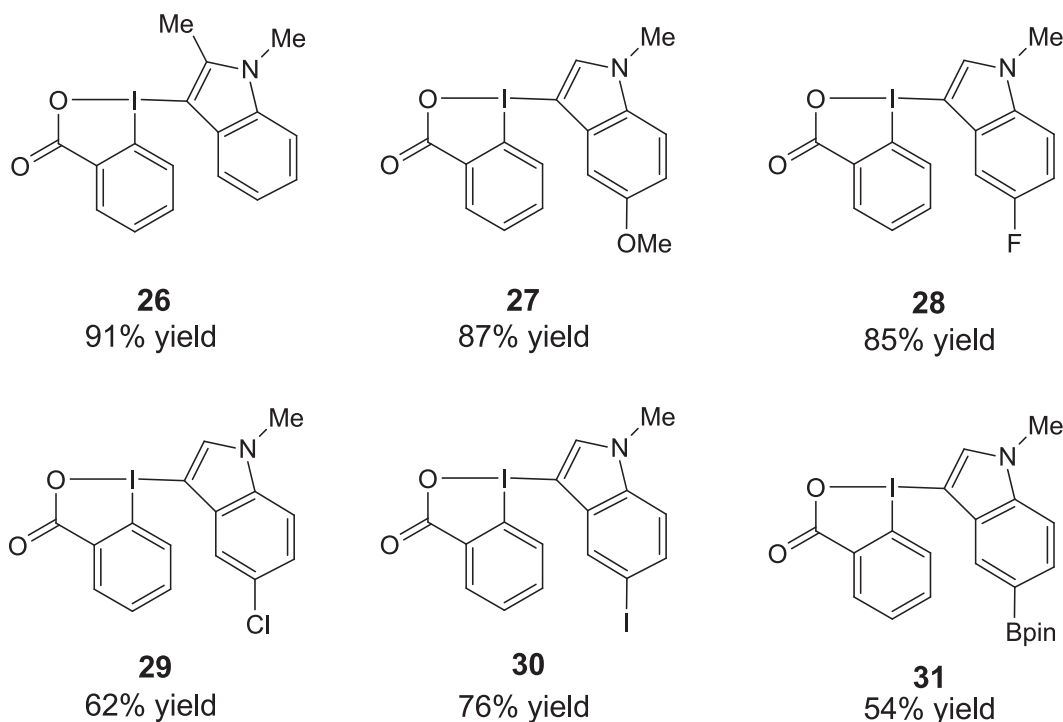
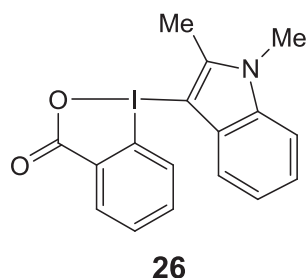


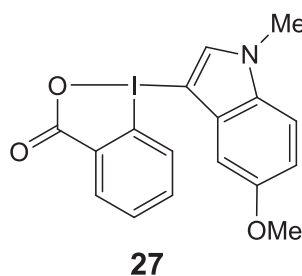
Figure S2: Scope of Heterocyclic-BX reagents (2)

1-(3-1,2-Dimethyl-1*H*-indole)-1*H*-1 λ_3 -benzo[*b*]iodo-3(2*H*)-one (26)



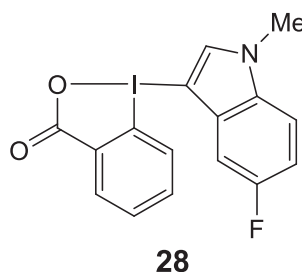
Following procedure A: starting from 2-methyl-1-methyl-1*H*-indole **106** (145 mg, 1.00 mmol), after 16 hours 1-(3-1,2-dimethyl-1*H*-indole)-1*H*-1 λ_3 -benzo[*b*]iodo-3(2*H*)-one **26** (364 mg, 0.930 mmol, 93% yield) was obtained as a dark violet foam. **Rf**: 0.43 (DCM:MeOH 9:1). **IR** ν 3055 (w), 2987 (w), 2948 (w), 1717 (w), 1605 (s), 1584 (m), 1553 (m), 1516 (w), 1472 (w), 1437 (w), 1395 (m), 1378 (m), 1268 (m), 1154 (w), 1032 (w), 1011 (w), 829 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.42 (dd, J = 7.3, 1.7 Hz, 1H, Ar*H*), 7.52 (td, J = 7.3, 0.9 Hz, 1H, Ar*H*), 7.44 (d, J = 8.2 Hz, 1H, Ar*H*), 7.35 (m, 2H, Ar*H*), 7.28 (m, 1H, Ar*H*), 7.23 (ddd, J = 8.2, 6.9, 1.0 Hz, 1H, Ar*H*), 6.77 (m, 1H, Ar*H*), 3.91 (s, 3H, CH₃N), 2.65 (s, 3H, ICH=CHCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 166.8, 145.3, 137.9, 133.7, 133.2, 132.7, 130.5, 128.9, 124.7, 123.6, 122.4, 119.2, 115.5, 110.4, 80.1, 31.1, 13.2. **HR-ESI-MS** 392.0146 ([M+H]⁺, C₁₇H₁₅INO₂⁺; calc. for 392.0142). The structure of the obtained regioisomer was assigned by NMR correlation to compound **25**.

1-(3-5-Methoxy-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (27)



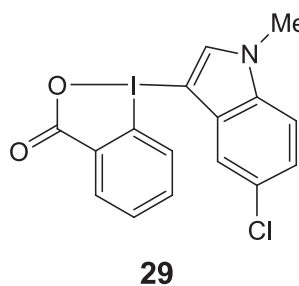
Following procedure **A**: starting from 5-methoxy-1-methyl-1*H*-indole **107** (161 mg, 1.00 mmol), after 16 hours 1-(3-5-methoxy-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **27** (346 mg, 0.850 mmol, 85% yield) was obtained as an orange resin. **Rf**: 0.42 (DCM:MeOH 9:1). **IR** ν 3110 (w), 3062 (w), 3000 (w), 2944 (w), 2837 (w), 1719 (w), 1604 (m), 1584 (m), 1556 (w), 1504 (m), 1489 (m), 1439 (w), 1378 (w), 1249 (s), 1223 (s), 1158 (m), 1031 (s), 970 (w), 845 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.35 (dd, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 7.82 (s, 1H, NCHCl), 7.48 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.40 (d, *J* = 9.0 Hz, 1H, Ar*H*), 7.27 (m, 1H, Ar*H*), 7.04 (dd, *J* = 9.0, 2.4 Hz, 1H, Ar*H*), 6.84 (d, *J* = 8.3 Hz, 1H, Ar*H*), 6.79 (d, *J* = 2.3 Hz, 1H, Ar*H*), 3.99 (s, 3H, CH₃N), 3.78 (s, 3H, OCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 167.1, 156.4, 138.9, 133.3, 132.5, 132.5, 130.5, 130.1, 125.2, 116.0, 114.8, 111.7, 100.8, 77.4, 55.8, 34.0 (*the signal for one aromatic C could not be resolved*). **HR-ESI-MS** 408.0093 ([M+H]⁺, C₁₇H₁₅INO₃⁺ calc. for 408.0091). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 25.*

1-(3-5-Fluoro-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (28)



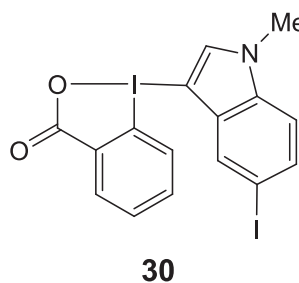
Following procedure **A**: starting from 5-fluoro-1-methyl-1*H*-indole **108** (149 mg, 1.00 mmol), after 16 hours 1-(3-5-fluoro-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **28** (336 mg, 0.850 mmol, 85% yield) was obtained as an yellow foam. **Rf**: 0.3 (DCM:MeOH 9:1). **IR** ν 3083 (w), 2952 (w), 1717 (w), 1601 (s), 1557 (m), 1503 (m), 1485 (m), 1438 (w), 1338 (m), 1242 (m), 1193 (m), 1121 (m), 1032 (w), 1005 (w), 850 (m). **¹H NMR** (400 MHz, CD₃OD) δ 8.14 (dd, *J* = 7.6, 1.7 Hz, 1H, Ar*H*), 8.01 (s, 1H, NCHCl), 7.57 (ddd, *J* = 8.8, 4.2, 0.8 Hz, 1H, Ar*H*), 7.49 (td, *J* = 7.4, 1.0 Hz, 1H, Ar*H*), 7.30 (ddd, *J* = 8.3, 7.2, 1.7 Hz, 1H, Ar*H*), 7.14 – 7.03 (m, 2H, Ar*H*), 6.80 (dd, *J* = 8.3, 0.9 Hz, 1H, Ar*H*), 3.93 (s, 3H, CH₃N). **¹³C NMR** (101 MHz, CD₃OD) δ 170.3, 160.91 (d, *J* = 238.2 Hz), 142.6, 135.9, 135.1, 134.4, 133.2, 131.7, 131.40 (d, *J* = 10.7 Hz), 127.7, 116.8, 113.71 (d, *J* = 9.8 Hz), 113.47 (d, *J* = 26.7 Hz), 105.67 (d, *J* = 25.3 Hz), 77.5, 34.3. **¹⁹F NMR** (376 MHz, CDCl₃) δ -119.8. **HR-ESI-MS** 395.9894 ([M+H]⁺, C₁₆H₁₂FINO₂⁺; calc. for 395.9891). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 25.*

1-(3-5-Chloro-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (29)



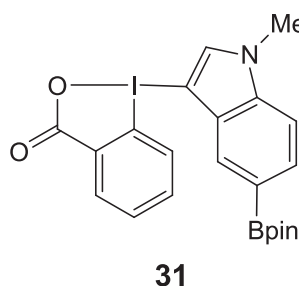
Following procedure A: starting from 5-chloro-1-methyl-1*H*-indole **109** (166 mg, 1.00 mmol), after 16 hours 1-(3-5-chloro-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **29** (256 mg, 0.622 mmol, 62% yield) was obtained as an orange amorphous solid. **Rf**: 0.4 (DCM:MeOH 9:1). **IR** ν 3095 (w), 2953 (w), 1605 (s), 1556 (m), 1505 (m), 1438 (m), 1388 (m), 1370 (m), 1260 (s), 1226 (m), 1164 (m), 1144 (m), 1115 (w), 1070 (w), 1032 (s), 1004 (w), 837 (w). **¹H NMR** (400 MHz, CD₂Cl₂) δ 8.20 (d, *J* = 7.4 Hz, 1*H*, Ar*H*), 7.78 (s, 1*H*, NCHCl), 7.38 (d, *J* = 8.7 Hz, 1*H*, Ar*H*), 7.34 – 7.22 (m, 3*H*, Ar*H*), 7.17 (t, *J* = 7.7 Hz, 1*H*, Ar*H*), 6.68 (d, *J* = 8.2 Hz, 1*H*, Ar*H*), 3.87 (s, 3*H*, CH₃NCHCl). **¹³C NMR** (101 MHz, MeOD) δ 170.3, 142.5, 137.8, 135.1, 134.4, 133.2, 131.7, 131.7, 129.6, 127.8, 125.4, 120.0, 116.8, 113.7, 77.5, 34.2. **HR-ESI-MS** 411.9603 ([*M*+*H*]⁺, C₁₆H₁₂ClINO₂⁺; calc. for 411.9596). The structure of the obtained regioisomer was assigned by NMR correlation to compound **25**.

1-(3-5-Iodo-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (30)



Following procedure A: starting from 5-iodo-1-methyl-1*H*-indole **110** (257 mg, 1.00 mmol), after 16 hours 1-(3-5-iodo-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **30** (380 mg, 0.755 mmol, 76% yield) was obtained as a yellow amorphous solid. **NB: the reagent is unstable in acidic deuterated solvents and it decompose in short time, we recommend the immediate use after the synthesis. The proton NMR presents about 21% of the open protonated form.** **Rf**: 0.3 (DCM:MeOH 9:1). **IR** ν 3092 (w), 3061 (w), 1600 (s), 1584 (m), 1557 (m), 1503 (m), 1436 (w), 1422 (w), 1371 (m), 1265 (s), 1245 (s), 1225 (m), 1163 (m), 1113 (w), 1031 (s), 1004 (w), 836 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.24 (m, 1*H*, Ar*H*), 7.83 (s, 1*H*, NCHCl), 7.58 – 7.47 (m, 2*H*, Ar*H*), 7.26 (m, 1*H*, Ar*H* + CDCl₃), 7.21 – 7.18 (m, 2*H*, Ar*H*), 6.67 (d, *J* = 8.1 Hz, 1*H*, Ar*H*), 3.87 (s, 3*H*, CH₃N). **¹³C NMR** (101 MHz, CDCl₃) δ 168.6, 140.5, 136.8, 133.7, 132.6, 132.3, 131.4, 130.3, 128.1, 126.0, 122.3, 119.1, 115.7, 112.9, 86.1, 34.0. **HR-ESI-MS** 503.8952 ([*M*+*H*]⁺, C₁₆H₁₂I₂NO₂⁺; calc. for 503.8952). The structure of the obtained regioisomer was assigned by NMR correlation to compound **25**.

1-(3-1-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole)-1*H*-1λ₃ - benzo[*b*]iodo-3(2*H*)-one (31)



Following procedure **A**: starting from commercially available 1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (149 mg, 1.00 mmol), after 16 hours 1-(3-1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole)-1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one **31** (276 mg, 0.549 mmol, 54% yield) was obtained as an orange amorphous solid. **Rf**: 0.46 (DCM:MeOH 9:1). **IR** ν 3095 (w), 2979 (w), 1611 (s), 1558 (w), 1507 (w), 1436 (w), 1360 (s), 1303 (w), 1263 (w), 1142 (s), 1114 (w), 1074 (w), 970 (w), 861 (w). **¹H NMR** (400 MHz, CD₂Cl₂) δ 8.32 (dd, J = 7.5, 1.7 Hz, 1H, Ar*H*), 7.93 (s, 1H, NCHCl), 7.81 (dd, J = 8.4, 1.1 Hz, 1H, Ar*H*), 7.74 (s, 1H, CCHCBPin), 7.59 – 7.48 (m, 2H, Ar*H*), 7.31 (ddd, J = 8.6, 7.1, 1.7 Hz, 1H, Ar*H*), 6.85 (dd, J = 8.3, 0.9 Hz, 1H, Ar*H*), 3.99 (s, 3H, NCH₃), 1.30 (s, 12H, CBPin). **¹³C NMR** (101 MHz, CD₂Cl₂) δ 167.0, 140.1, 139.6, 134.1, 133.8, 132.6, 131.0, 130.5, 129.5, 127.6, 126.0, 117.1, 110.7, 84.5, 80.3, 34.4, 25.2 (one aromatic Carbon signal not resolved). **HR-ESI-MS** 504.0835 ([M+H]⁺, C₂₂H₂₄BINO₄⁺; calc. for 504.0838). The structure of the obtained regioisomer was assigned by NMR correlation to compound **25**.

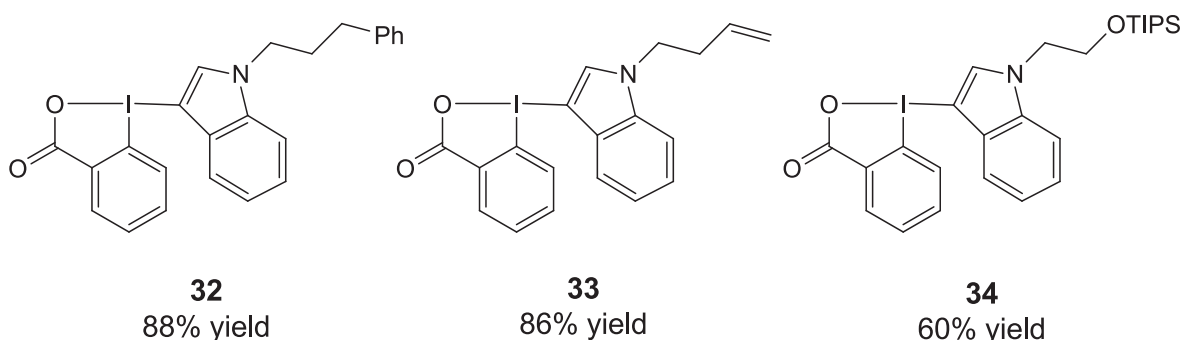
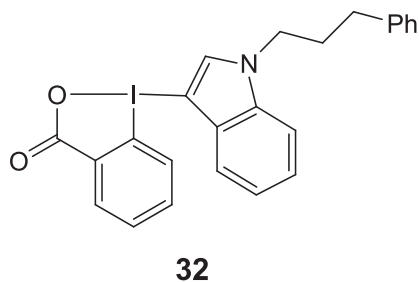


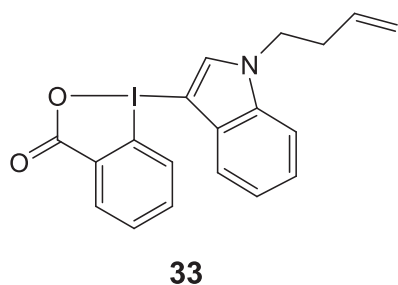
Figure S3: Scope of Heterocyclic-BX reagents (3)

1-(3-1-(3-Phenylpropyl)-1*H*-indole)-1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one (32)



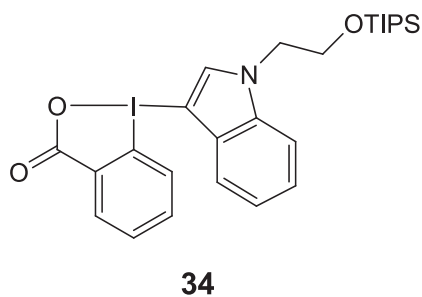
Following procedure **A**: starting from 1-(3-phenylpropyl)-indole **114** (235 mg, 1.00 mmol), after 16 hours 1-(3-1-(3-phenylpropyl)-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **32** (436 mg, 0.906 mmol, 91% yield) was obtained as an orange resin. **Rf**: 0.45 (DCM:MeOH 9:1). **IR** ν 3060 (w), 3026 (w), 2939 (w), 1717 (w), 1601 (s), 1551 (m), 1498 (m), 1455 (w), 1364 (w), 1245 (w), 1165 (w), 1005 (w), 828 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.37 (dd, *J* = 7.5, 1.7 Hz, 1*H*, Ar*H*), 7.86 (s, 1*H*, NCHCl), 7.54 – 7.36 (m, 4*H*, Ar*H*), 7.33 – 7.19 (m, 5*H*, Ar*H*), 7.18 – 7.14 (m, 2*H*, Ar*H*), 6.79 (dd, *J* = 8.3, 0.8 Hz, 1*H*, Ar*H*), 4.34 (t, *J* = 7.2 Hz, 2*H*, NCH₂), 2.73 (t, *J* = 7.5 Hz, 2*H*, CH₂Ph), 2.35 (m, 2*H*, CH₂-CH₂-CH₂). **¹³C NMR** (101 MHz, CDCl₃) δ 166.8, 140.0, 137.8, 136.8, 133.4, 133.2, 132.4, 130.4, 129.3, 128.6, 128.3, 126.4, 125.2, 124.1, 122.5, 120.0, 116.1, 110.9, 78.9, 46.7, 32.8, 31.1. **HR-ESI-MS** 482.0614 ([*M*+*H*]⁺, C₂₄H₂₁INO₂⁺; calc. for 482.0612). The structure of the obtained regioisomer was assigned by NMR correlation to compound **25**.

1-(3-1-(But-3-en-1-yl)-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (**33**)



Following procedure **A**: starting from 1-(but-3-en-1-yl)-1*H*-indole **112** (171 mg, 1.00 mmol), after 16 hours 1-(3-1-(but-3-en-1-yl)-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **33** (359 mg, 0.860 mmol, 86% yield) was obtained, as a yellow amorphous solid. **Rf**: 0.44 (DCM:MeOH 9:1). **IR** ν 3082 (w), 1607 (s), 1557 (m), 1500 (m), 1456 (w), 1437 (w), 1389 (w), 1358 (m), 1262 (w), 1160 (w), 1005 (w), 919 (w), 830 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.35 (dd, *J* = 7.4, 1.7 Hz, 1*H*, Ar*H*), 7.91 (s, 1*H*, NCHCl), 7.54 (m, 1*H*, Ar*H*), 7.49 (td, *J* = 7.3, 0.9 Hz, 1*H*, Ar*H*), 7.46 – 7.39 (m, 2*H*, Ar*H*), 7.32 – 7.19 (m, 2*H*, Ar*H*), 6.73 (dd, *J* = 8.3, 0.9 Hz, 1*H*, Ar*H*), 5.82 (ddt, *J* = 17.1, 10.3, 6.9 Hz, 1*H*, NCH₂CH₂CH=CH₂), 5.12 – 4.97 (m, 2*H*, NCH₂CH₂CH=CH₂), 4.41 (t, *J* = 6.9 Hz, 2*H*, NCH₂), 2.71 (m, 2*H*, CH₂). **¹³C NMR** (101 MHz, CDCl₃) δ 166.8, 137.9, 136.7, 133.6, 133.4, 133.2, 132.5, 130.5, 129.4, 125.2, 124.2, 122.5, 120.0, 118.6, 116.2, 110.9, 79.0, 46.9, 34.2. **HR-ESI-MS** 418.0294 ([*M*+*H*]⁺, C₁₉H₁₇INO₂⁺; calc. for 418.0299). The structure of the obtained regioisomer was assigned by NMR correlation to compound **25**.

1-(3-1-(2-((Triisopropylsilyl)oxy)ethyl)-1*H*-indole)-1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one (34)



Following procedure **A**: starting from 1-(2-((triisopropylsilyl)oxy)ethyl)-1*H*-indole **113** (318 mg, 1.00 mmol), after 16 hours 1-(3-1-(2-((triisopropylsilyl)oxy)ethyl)-1*H*-indole)-1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one **34** (873 mg, 0.929 mmol, 60% yield) was obtained as an orange oil. **R_f**: 0.40 (DCM:MeOH 9:1). **IR** ν 2942 (w), 2890 (w), 2865 (m), 1716 (w), 1604 (s), 1555 (w), 1500 (w), 1458 (w), 1358 (m), 1249 (m), 1169 (w), 1115 (w), 1015 (w), 883 (m), 831 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.47 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.99 (s, 1H, NCHCl), 7.65 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.59 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.51 – 7.45 (m, 2H, Ar*H*), 7.35 (m, 2H, Ar*H*), 6.94 (d, *J* = 8.3 Hz, 1H, Ar*H*), 4.54 (t, *J* = 5.0 Hz, 2H, CH₂), 4.20 (t, *J* = 5.0 Hz, 2H, CH₂), 1.09 (dd, *J* = 8.7, 5.6 Hz, 3H, SiCH(CH₃)₂), 1.01 (d, *J* = 7.1 Hz, 18H, SiCH(CH₃)₂). **¹³C NMR** (101 MHz, CDCl₃) δ 167.0, 138.8, 137.1, 133.2, 133.2, 132.4, 130.4, 129.1, 125.3, 124.0, 122.4, 119.7, 115.8, 111.0, 78.3, 62.3, 49.8, 17.7, 11.6. **HR-ESI-MS** 564.1431 ([M+H]⁺, C₂₆H₃₅INO₃Si⁺; calc. for 564.1425). The structure of the obtained regioisomer was assigned by NMR correlation to compound **25**.

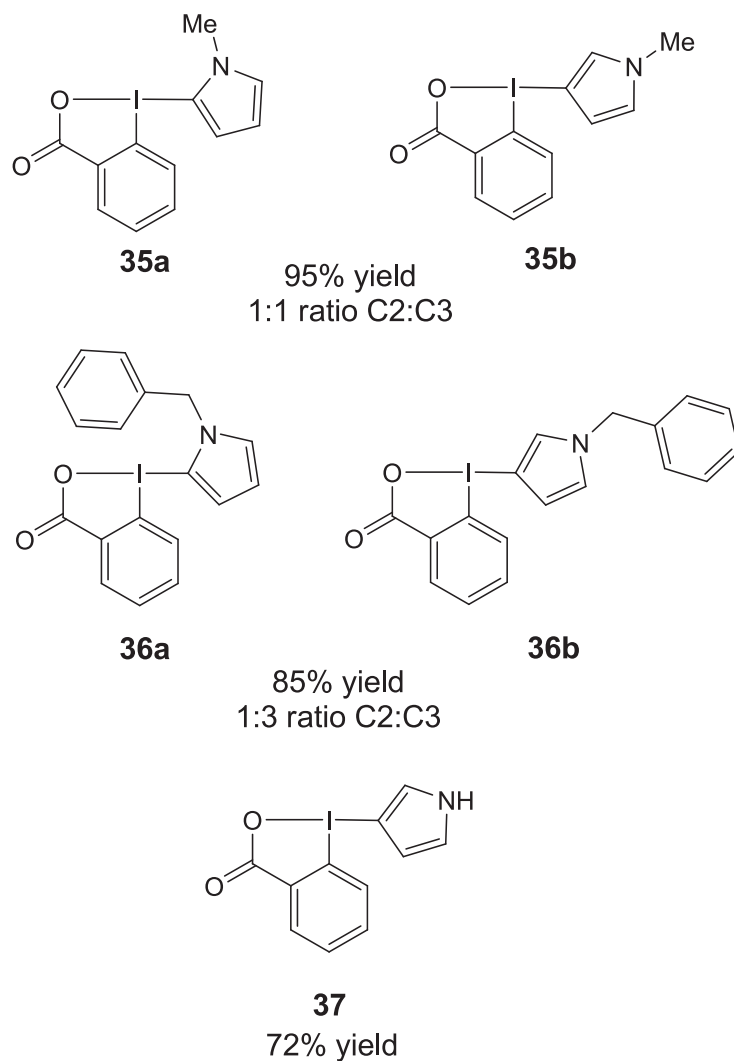
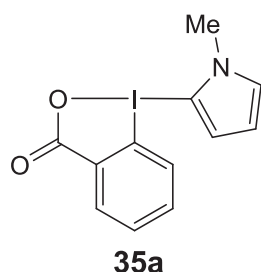


Figure S4: Scope of Heterocyclic-BX reagents (4)

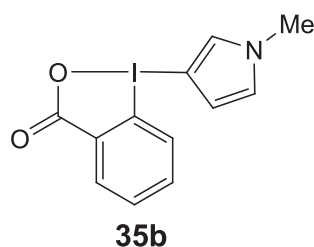
1-(2-1-Methyl-1*H*-pyrrole)-1*H*-1 λ_3 -benzo[*b*]iodo-3(2*H*)-one (35a) and 1-(3-1-methyl-1*H*-pyrrole)-1*H*-1 λ_3 -benzo[*b*]iodo-3(2*H*)-one (35b).

Following procedure **A**: starting from commercially available 1-methyl-1*H*-pyrrole **12** (0.890 ml, 1.00 mmol), after 12 hours 1-(2-1-methyl-1*H*-pyrrole)-1*H*-1 λ_3 -benzo[*b*]iodo-3(2*H*)-one **35a** and 1-(3-1-methyl-1*H*-pyrrole)-1*H*-1 λ_3 -benzo[*b*]iodo-

3(2*H*)-one **35b** were obtained as a 1:1 mixture (310 mg, 0.948 mmol, overall yield 95%) as an off-white, sticky amorphous solid. Rf: 0.5 (DCM:MeOH 9:1). The two compounds were separated by slow flash column chromatography (EtOAc:MeOH 9:1). *The structure of the obtained regioisomers were assigned by NMR correlation to compound 37.*

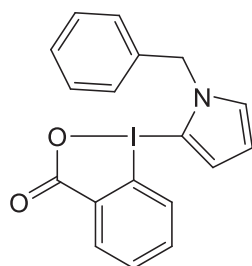


1-(2-1-methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **35a** (152 mg, 0.465 mmol, 47% yield; off-white, sticky amorphous solid) **Rf**: 0.3 (EtOAc:MeOH 9:1). **IR** ν 3415 (w), 3105 (w), 3049 (w), 2950 (w), 1604 (s), 1584 (m), 1558 (w), 1508 (w), 1437 (w), 1346 (m), 1288 (m), 1223 (w), 1149 (w), 1091 (w), 1047 (w), 1005 (w), 829 (m). **¹H NMR** (400 MHz, CD₃OD) δ 8.24 (dd, *J* = 7.5, 1.6 Hz, 1*H*, Ar*H*), 7.65 (td, *J* = 7.4, 1.0 Hz, 1*H*, Ar*H*), 7.55 (m, 1*H*, Ar*H*), 7.27 (t, *J* = 2.1 Hz, 1*H*, Ar*H*), 7.01 (dd, *J* = 3.9, 1.6 Hz, 1*H*, Ar*H*), 6.72 (dd, *J* = 8.3, 1.0 Hz, 1*H*, Ar*H*), 6.43 (dd, *J* = 3.9, 2.1 Hz, 1*H*, Ar*H*), 3.78 (s, 1*H*, NCH₃). **¹³C NMR** (101 MHz, CD₃OD) δ 170.1, 135.5, 134.2, 133.2, 131.9, 131.4, 127.7, 126.6, 119.4, 112.9, 96.0, 37.4. **HR-ESI-MS** 327.9842 ([*M*+*H*]⁺, C₁₂H₁₁INO₂⁺; calc. for 327.9829). *DSC-analysis was performed on compound 35a: see par.5 of Supplementary informations.*

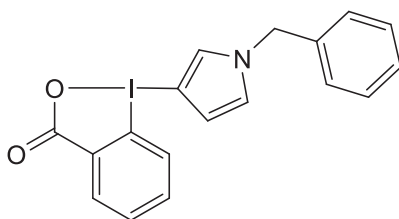


1-(3-1-methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **35b** (158 mg, 0.483 mmol, 48% yield; off-white, sticky amorphous solid). **Rf**: 0.25 (EtOAc:MeOH 9:1). **IR** ν 3447 (w), 3106 (w), 2947 (w), 2863 (w), 1603 (s), 1591 (m), 1558 (m), 1512 (m), 1437 (w), 1354 (m), 1294 (w), 1110 (m), 1083 (w), 1007 (w), 829 (m). **¹H NMR** (400 MHz, CD₃OD) δ 8.15 (dd, *J* = 7.5, 1.7 Hz, 1*H*, Ar*H*), 7.53 (td, *J* = 7.3, 1.1 Hz, 1*H*, Ar*H*), 7.49 – 7.40 (m, 2*H*, Ar*H*), 7.04 – 6.98 (m, 2*H*, Ar*H*), 6.58 (d, *J* = 1.2 Hz, 1*H*, Ar*H*), 3.85 (s, 3*H*, NMe). **¹³C NMR** (101 MHz, CD₃OD) δ 170.0, 134.9, 134.2, 133.4, 132.8, 131.5, 127.9, 127.7, 117.4, 116.6, 82.8, 37.1. **HR-ESI-MS** 327.9831 ([*M*+*H*]⁺, C₁₂H₁₁INO₂⁺; calc. for 327.9829). *DSC-analysis was performed on compound 35b: see par.5 of Supplementary informations.*

1-(2-1-benzyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (36a) and 1-(3-1-benzyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (36b)



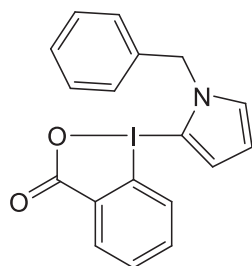
36a



36b

Following procedure **A**: starting from commercially available 1-benzyl-1*H*-pyrrole (0.890 ml, 1.00 mmol), after 12 hours 1-(2-(1-benzyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **36a** and 1-(3-(1-benzyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **36b** were

obtained in 3:1 mixture (345 mg, 0.856 mmol, overall yield 86%), as a colorless amorphous solid. **Rf**: 0.7 (DCM:MeOH 9:1). The two compounds were separated by slow flash column chromatography (EtOAc:MeOH 9:1). *The structure of the obtained regioisomers were assigned by NMR correlation to compound 37.*



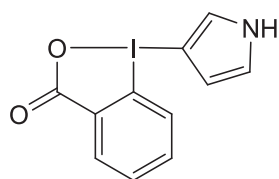
36a

1-(2-(1-benzyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **36a** (85.0 mg, 0.211 mmol, 21% yield); colorless foam. **Rf**: 0.5 (EtOAc:MeOH 9:1). **IR** ν 3109 (w), 3064 (w), 2968 (w), 2875 (w), 1609 (s), 1585 (m), 1558 (w), 1503 (w), 1456 (w), 1440 (w), 1357 (m), 1277 (w), 1103 (m), 1079 (w), 1032 (w), 1031 (w), 830 (w). **¹H NMR** (400 MHz, 2:1 mixture CD₃OD:C₆D₆, referered to CD₃OD) δ 8.18 (dd, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 7.28 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.10 (t, *J* = 2.2 Hz, 1H, Ar*H*), 6.92 (m, *J* = 7.6, 2.9 Hz, 6H, Ar*H* + C₆D₆), 6.71 (dd, *J* = 3.9, 1.7 Hz, 1H, Ar*H*), 6.35 (t, *J* = 3.4 Hz, 1H, Ar*H*), 6.23 (d, *J* = 8.3 Hz, 1H, Ar*H*), 4.90 (s, 2H, NCH₂Ph). **¹³C NMR** (101 MHz, 2:1 mixture CD₃OD:C₆D₆, referered to CD₃OD) δ 169.8, 136.9, 134.6, 132.7, 131.2, 131.1, 129.5, 129.0, 128.5, 127.2, 119.2, 112.9, 94.8, 54.7 (two Carbon signals under the deuterated benzene). **HR-ESI-MS** 404.0140 ([*M*+*H*]⁺, C₁₈H₁₅INO₂⁺; calc. for 404.0142).

1-(3-(1-benzyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **36b** (260 mg, 0.645 mmol, 65% yield); colorless foam. **Rf**: 0.46 (EtOAc:MeOH 9:1). **IR** ν 3409 (w), 3114 (w), 2971 (w), 1609 (s), 1585 (m), 1558 (w), 1456 (w), 1438 (w), 1365 (m), 1277 (s), 1160 (w), 1079 (w), 1032 (m), 835 (w). **¹H NMR** (400 MHz,

2:1 mixture $CD_3OD:C_6D_6$, referred to CD_3OD) δ 8.29 (dd, $J = 7.5, 1.7$ Hz, 1H, ArH), 7.36 (t, $J = 7.3$ Hz, 1H, ArH), 7.30 – 7.20 (m, 3H ArH + C_6D_6), 7.18 – 7.08 (m, 3H, ArH), 6.97 (d, $J = 2.0$ Hz, 1H, ArH), 6.83 – 6.78 (m, 2H, ArH), 6.30 (dd, $J = 3.0, 1.7$ Hz, 1H, ArH), 4.93 (s, 2H, NCH_2Ph). ^{13}C NMR (101 MHz, 2:1 mixture $CD_3OD:C_6D_6$, referred to CD_3OD) δ 168.7, 136.8, 133.5, 133.0, 131.8, 130.9, 130.3, 128.8, 128.1, 127.4, 126.2, 125.5, 116.3, 115.3, 82.4, 53.5. **HR-ESI-MS** 404.0140 ($[M+H]^+$, $C_{18}H_{15}INO_2^+$; calc. for 404.0142).

1-(3-1H-Pyrrole)-1H-1*λ*₃-benzo[*b*]iodo-3(2H)-one (37)



37

Following procedure **A**: starting from 1-(*tert*-butyldimethylsilyl)-1H-pyrrole **111** (181 mg, 1.00 mmol) and using $Sc(OTf)_3$ as the Lewis Acid (20 mol%), after 16 hours 1-(3-1H-pyrrole)-1H-1*λ*₃-benzo[*b*]iodo-3(2H)-one **9n** (225 mg, 0.719 mmol, 72% yield) was obtained as a slightly brown solid. **Rf**: 0.5 (DCM:MeOH 9:1). **Mp**: 147°C (decomposition). **IR** ν 3484 (w), 1607 (w), 1558 (w), 1439 (w), 1397 (w), 1260 (s), 1236 (s), 1174 (s), 1084 (w), 1050 (m), 1038 (m), 903 (w), 882 (w). 1H NMR (400 MHz, MeOD) δ 8.40 (dd, $J = 7.5, 1.7$ Hz, 1H, ArH), 7.72 (d, $J = 7.4$ Hz, 1H, ArH), 7.68 – 7.59 (m, 2H, ArH), 7.23 (t, $J = 2.4$ Hz, 1H, ArH), 7.14 (d, $J = 8.2$ Hz, 1H, ArH), 6.74 (dd, $J = 2.8, 1.5$ Hz, 1H, ArH) (*NH* signal exchanges with MeOD). ^{13}C NMR (101 MHz, MeOD) δ 170.3, 135.0, 134.4, 132.9, 131.5, 130.4, 128.0, 123.7, 117.3, 115.9, 83.4. **HRMS** (ESI) calcd for $C_{11}H_9INO_2^+$ $[M+H]^+$ 313.9673; found 313.9673. The structure of the reagent was assigned based on X-Ray diffraction (CCDC number **1541174**).

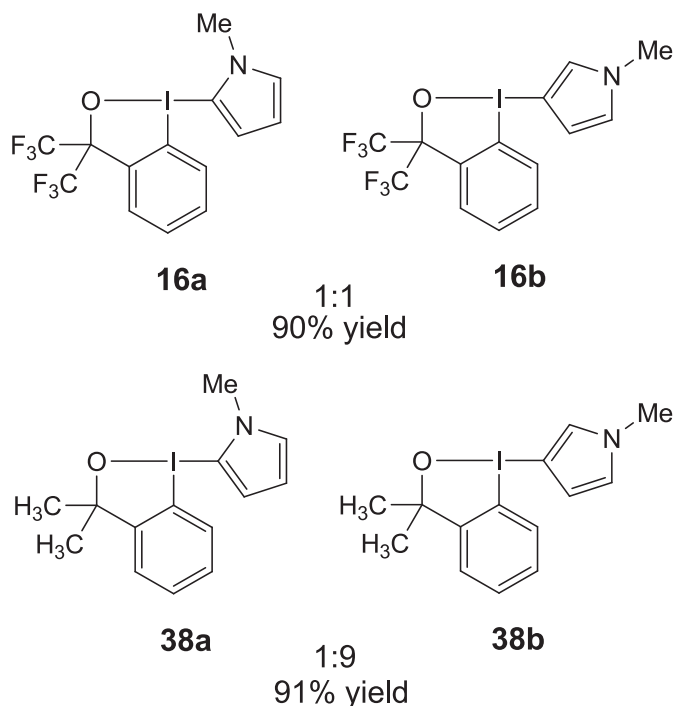
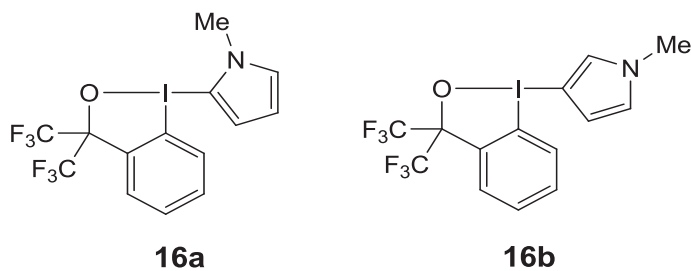


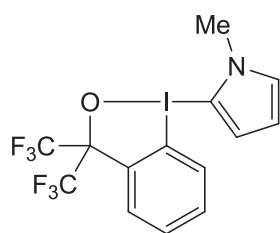
Figure S5: Scope of Heterocyclic-BX reagents (5)

1-(2-1-Methyl-1*H*-pyrrole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ³-benzo[*d*][1,2]iodaoxole (16a) and 1-(3-1-methyl-1*H*-pyrrole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ³-benzo[*d*][1,2]iodaoxole (16b)



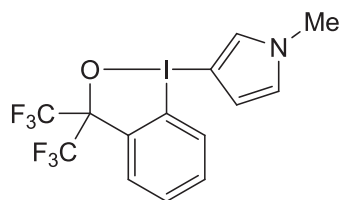
Following procedure **B**: starting from commercially available 1-methyl-1*H*-pyrrole **12** (17.8 μl, 0.200 mmol) and 1-acetoxy-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole **18** (94.0 mg, 0.220 mmol, 1.10 equiv.),

after 12 hours 1-(2-1-methyl-1*H*-pyrrole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ³-benzo[*d*][1,2]iodaoxole **16a** and 1-(3-1-methyl-1*H*-pyrrole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ³-benzo[*d*][1,2]iodaoxole **16b** were obtained in 1:1 mixture (81.5 mg, 182 mmol, overall yield 90%), as a slightly grey amorphous solid. Rf: 0.5 (DCM:MeOH 9:1). The two compounds were separated by slow flash column chromatography (EtOAc:MeOH 20:1). *The structure of the obtained regioisomers were assigned by NMR correlation to compound 37.*



16a

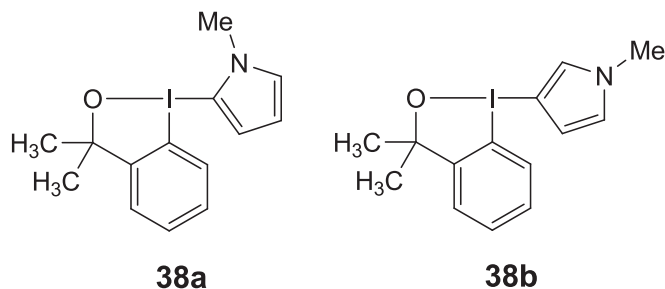
1-(2-1-methyl-1*H*-pyrrole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ³-benzo[*d*][1,2]iodaoxole **16a** (41.2 mg, 92.0 μmol, 45% yield); colorless foam. **Rf**: 0.50 (EtOAc:MeOH 9:1). **IR** ν 3734 (w), 3702 (w), 3628 (w), 1716 (w), 1509 (w), 1459 (w), 1288 (m), 1265 (s), 1214 (m), 1181 (s), 1158 (s), 966 (m), 951 (m), 914 (w). **¹H NMR** (400 MHz, CDCl₃) δ 7.86 (dd, *J* = 7.7, 1.3 Hz, 1H, *ArH*), 7.57 (td, *J* = 7.4, 1.1 Hz, 1H, *ArH*), 7.41 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H, *ArH*), 6.97 (dd, *J* = 2.7, 1.6 Hz, 1H, *ArH*), 6.78 (dd, *J* = 3.8, 1.6 Hz, 1H, *ArH*), 6.63 (dd, *J* = 8.3, 1.1 Hz, 1H, *ArH*), 6.34 (dd, *J* = 3.8, 2.7 Hz, 1H, *ArH*), 3.68 (s, 3H, *NCH*₃). **¹³C NMR** (101 MHz, CDCl₃) δ 132.3, 131.3, 130.5, 130.2, 128.3, 126.4, 124.2, 122.6 (m), 114.3, 111.3, 102.5, 81.40 (dt, *J* = 57.9, 29.6 Hz), 37.0. **HR-APCI-MS** 449.9771 ([*M*+*H*]⁺, C₁₄H₁₁F₆INO⁺; calc. for 449.9784). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 37.*



16b

1-(3-1-methyl-1*H*-pyrrole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ³-benzo[*d*][1,2]iodaoxole **16b** (40.3 mg, 90.0 μmol, 45% yield); slightly grey amorphous foam. **Rf**: 0.48 (EtOAc:MeOH 9:1). **IR** ν 2938 (w), 2929 (w), 1718 (w), 1510 (w), 1464 (w), 1264 (s), 1181 (s), 1161 (s), 1108 (w), 966 (m), 949 (m). **¹H NMR** (400 MHz, CDCl₃) δ 7.82 (m, 1H, *ArH*), 7.52 (ddd, *J* = 7.8, 7.1, 1.1 Hz, 1H, *ArH*), 7.37 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H, *ArH*), 7.08 (dd, *J* = 8.3, 1.1 Hz, 1H, *ArH*), 6.99 (t, *J* = 1.9 Hz, 1H, *ArH*), 6.76 (dd, *J* = 2.7, 2.1 Hz, 1H, *ArH*), 6.42 (dd, *J* = 2.8, 1.7 Hz, 1H, *ArH*), 3.80 (s, 3H, *NCH*₃). **¹³C NMR** (101 MHz, CDCl₃) δ 131.6, 131.3, 130.4, 129.9, 129.8, 126.9, 125.38, 124.19 (q, *J* = 291.5 Hz), 115.77, 112.69, 89.21, 81.47 (p, *J* = 28.7 Hz), 36.65. **HR-APCI-MS** 449.9771 ([*M*+*H*]⁺, C₁₄H₁₁F₆INO⁺; calc. for 449.9784). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 37.*

1-(2-1-Methyl-1*H*-pyrrole)-3,3-dimethyl-1,3-dihydro-1 λ^3 -benzo[*d*][1,2]iodoxole (38a) and 1-(3-1-methyl-1*H*-pyrrole)-3,3-dimethyl-1,3-dihydro-1 λ^3 -benzo[*d*][1,2]iodoxole (38b)



Following procedure **B**: starting from commercially available 1-methyl-1*H*-pyrrole **12** (17.8 μ l, 0.200 mmol) and 3,3-dimethyl-1 λ^3 -benzo[*d*][1,2]iodoxol-1(3*H*)-yl acetate **22** (70.4 mg, 0.220 mmol, 1.10 equiv.), after 12 hours 1-(2-1-Methyl-1*H*-

pyrrole)-3,3-dimethyl-1,3-dihydro-1 λ^3 -benzo[*d*][1,2]iodoxole **38a** and 1-(3-1-methyl-1*H*-pyrrole)-3,3-dimethyl-1,3-dihydro-1 λ^3 -benzo[*d*][1,2]iodoxole **38b** were obtained in 1:9 unseparable mixture (62.0 mg, 0.182 mmol, overall yield 91%), as a slightly grey amorphous solid. Rf: 0.4 (DCM:MeOH 20:1). **NB: the reagent is unstable in acidic deuterated solvents and it decompose in short time, we recommend the immediate use after the synthesis. The proton and carbon NMRs present about 2% of the open protonated alcohol form.** IR ν 3115 (w), 2986 (w), 1614 (w), 1509 (w), 1455 (w), 1372 (w), 1284 (s), 1247 (s), 1225 (m), 1163 (m), 1110 (w), 1031 (s), 992 (w). **¹H NMR** (400 MHz, CD₂Cl₂) on a *maj:min* (9:1) δ 7.53 (m, 0.26H, 2 Ar*H min*), 7.50 (dd, *J* = 7.0, 1.0 Hz, 1H, Ar*H maj*), 7.45 (dd, *J* = 7.8, 1.8 Hz, 1H, Ar*H maj*), 7.33 (t, *J* = 2.0 Hz, 1H, Ar*H maj*), 7.28 (dtd, *J* = 8.7, 7.0, 6.5, 1.8 Hz, 1.24H, Ar*H maj* + 2*H ArH min*), 7.23 (dd, *J* = 2.9, 1.7 Hz, 0.12H,), 7.04 (dd, *J* = 8.4, 1.1 Hz, 1H, Ar*H maj*), 6.94 (dd, *J* = 2.9, 2.1 Hz, 1H, Ar*H maj*), 6.66 (dd, *J* = 8.4, 0.9 Hz, 0.12H, Ar*H min*), 6.57 (dd, *J* = 3.0, 1.8 Hz, 1H, Ar*H maj*), 6.48 (dd, *J* = 4.1, 2.8 Hz, 0.12H, Ar*H min*), 3.85 (s, 3.32H, NCH₃ *maj+min*), 1.68 (s, 6.73H, N(CH₃)₂ *maj+min*). **Major regioisomer C3 X:** **¹³C NMR** (101 MHz, CD₂Cl₂) δ 146.4, 133.4, 131.5, 131.0, 129.0, 127.7, 127.7, 116.5, 109.9, 77.8, 75.1, 37.8, 30.8. **Minor regioisomer C2 X:** **¹³C NMR** (101 MHz, CD₂Cl₂) δ 146.6, 132.6, 131.9, 129.5, 128.4, 127.4, 122.6, 119.4, 113.6, 89.3, 75.4, 37.9, 30.8. (the last two overlap with the major regioisomers). **HR-ESI-MS** 342.0350 ([*M*+*H*]⁺, C₁₄H₁₇INO⁺; calc. for 342.0349). The structure of the obtained regioisomer was assigned by NMR correlation to compound **37**.

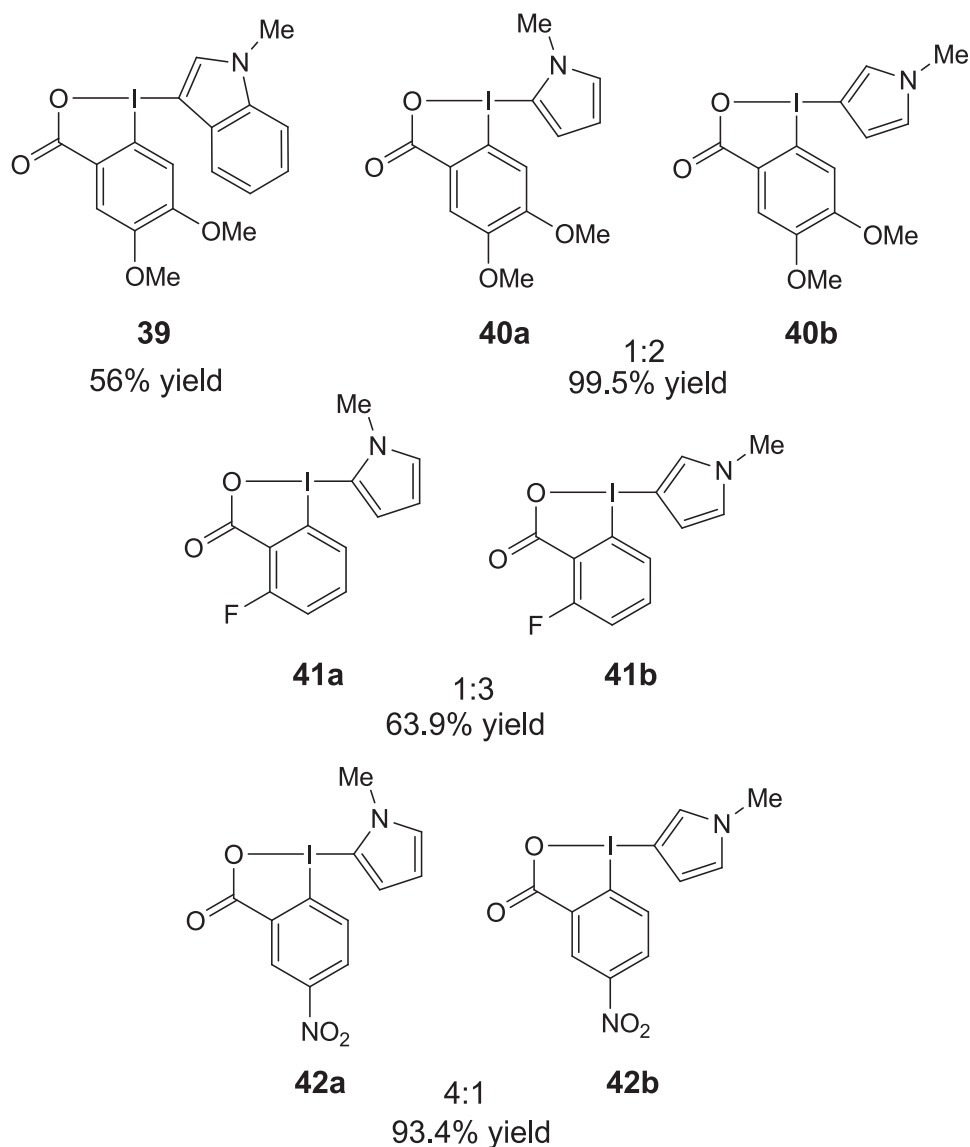


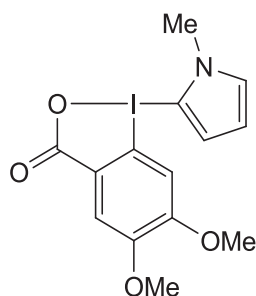
Figure S6: Scope of Heterocyclic-BX reagents (6)

5,6-Dimethoxy-1-(3-1-Methyl-1*H*-indole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one (39)

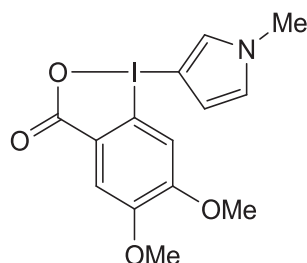
Following procedure **B**: starting from commercially available 1-methyl-1-*H*-indole **14** (26.2 mg, 0.100 mmol) and 5,6-dimethoxy-3-oxobenzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate **95** (81.0 mg, 0.220 mmol, 1.10 equiv.), after 16 hours 1-(3-1-methyl-1*H*-indole)-3,3-dimethyl-1,3-dihydro-1λ³-benzo[*d*][1,2]iodoxole **39** (49.0 mg, 0.112 mmol, 56% yield) was obtained as a brown foam. **Rf**: 0.7 (DCM:MeOH 9:1). **IR** ν 3113 (w), 2942 (w), 1603 (s), 1499 (s), 1455 (m), 1394 (s), 1330 (s), 1270 (s),

1212 (s), 1131 (m), 1017 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.04 (s, 1H, ArH), 7.73 (s, 1H, ArH), 7.53 – 7.47 (m, 1H, ArH), 7.43 (m, 1H, ArH), 7.40 (dd, *J* = 8.2, 1.2 Hz, 1H, ArH), 7.29 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H, ArH), 6.12 (s, 1H, ArH), 4.03 (s, 3H, Me), 3.87 (s, 3H, Me), 3.20 (s, 3H, Me). **¹³C NMR** (101 MHz, CDCl₃) δ 167.2, 153.2, 150.9, 139.3, 137.4, 129.1, 126.4, 124.2, 122.5, 119.9, 113.3, 110.6, 107.3, 104.9, 79.0, 56.3, 55.7, 33.9. **HR-ESI-MS** 438.0197 ([M+H]⁺, C₁₈H₁₇INO₄⁺; calc. for 438.0197). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 25.*

5,6-Dimethoxy-1-(2-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one (40a) and 5,6-dimethoxy-1-(3-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one (40b)



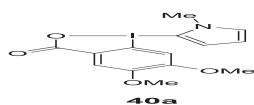
40a



40b

Following procedure **B**: starting from commercially available 1-methyl-1*H*-pyrrole **12** (17.8 μl, 0.200 mmol) and 5,6-dimethoxy-3-oxobenzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate **95** (81.0 mg, 0.220 mmol, 1.10 equiv.), after 12 hours 5,6-dimethoxy-1-(2-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one **40a**

and 5,6-dimethoxy-1-(3-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one **40b** were obtained in 1:2 mixture (77.0 mg, 0.199 mmol, overall yield 99%), as a yellow foam. R_f: 0.40 (DCM:MeOH 9:1). The two compounds were separated by slow flash column chromatography (EtOAc:MeOH 20:1). *The structure of the obtained regioisomers were assigned by NMR correlation to compound 37.*

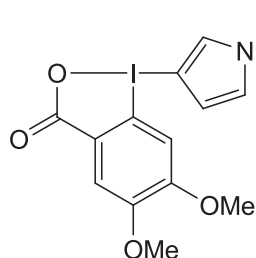


40a

5,6-dimethoxy-1-(2-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one **40a** (26.0 mg, 67.0 μmol, 33% yield); yellow foam. **R_f**: 0.40 (EtOAc:MeOH 9:1). **IR** ν 3104 (w), 2942 (w), 2848 (w), 1607 (s), 1562 (s), 1498 (s), 1392 (s), 1270 (s), 1212 (s), 1182 (m), 1019 (m). **¹H NMR** (400 MHz, CDCl₃) δ 7.88 (s, 1H, ArH), 7.07 (dd, *J* = 2.8, 1.6 Hz, 1H, ArH), 6.92 (dd, *J* = 3.9, 1.6 Hz, 1H, ArH), 6.42 (dd, *J* = 3.9, 2.8 Hz, 1H, ArH), 5.83 (s, 1H, ArH), 3.95 (s, 3H, Me), 3.76 (s, 3H, Me), 3.57 (s, 3H, Me). **¹³C NMR** (101 MHz, CDCl₃) δ 166.8, 154.1, 151.5, 129.3, 126.5, 125.3, 113.6, 112.1, 107.6,

106.2, 98.0, 56.6, 56.1, 37.4. **HR-ESI-MS** 388.0034 ($[M+H]^+$, $C_{14}H_{15}INO_4^+$; calc. for 388.0040).

The structure of the obtained regioisomer was assigned by NMR correlation to compound 37.

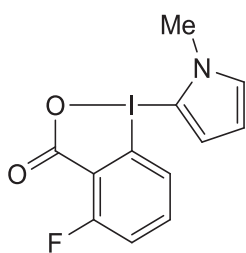


40b

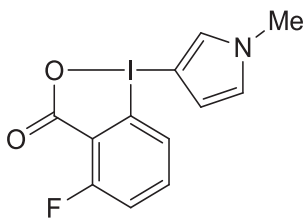
5,6-dimethoxy-1-(3-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one **40b** (51.0 mg, 0.132 mmol, 66% yield); yellow foam. **Rf**: 0.38 (EtOAc:MeOH 9:1). **IR** ν 3109 (w), 2941 (w), 2850 (w), 1609 (m), 1562 (s), 1498 (s), 1392 (s), 1326 (m), 1270 (s), 1212 (s), 1182 (w), 1128 (w), 1019 (m). **¹H NMR** (400 MHz, CDCl₃) δ 7.84 (s, 1*H*, Ar*H*), 7.25 (d, *J* = 1.9 Hz, 1*H*, Ar*H*), 6.84 (s, 1*H*, Ar*H*), 6.54 (m, 1*H*, Ar*H*), 6.36 (s, 1*H*, Ar*H*), 3.94 (s, 3*H*, Me), 3.85 (s, 3*H*, Me), 3.62 (s, 3*H*, Me). **¹³C NMR**

(101 MHz, CDCl₃) δ 167.0, 153.3, 151.0, 131.3, 126.6, 125.9, 115.7, 113.4, 107.3, 105.6, 85.0, 56.4, 56.0, 37.0. **HR-ESI-MS** 388.0035 ($[M+H]^+$, $C_{14}H_{15}INO_4^+$; calc. for 388.0040). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 37.*

4-Fluoro-1-(2-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one (41a) and 4-Fluoro-1-(3-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one (41b)



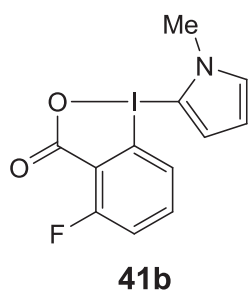
41a



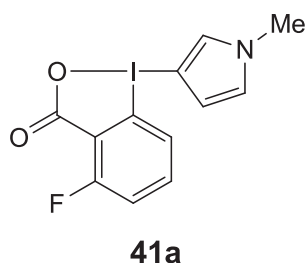
41b

Following procedure **B**: starting from commercially available 1-methyl-1*H*-pyrrole **12** (17.8 μl, 0.200 mmol) and 4-fluoro-3-oxo-1λ₃-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate **96** (71.3 mg, 0.220 mmol, 1.10 equiv.), after 12 hours 4-Fluoro-1-(2-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -

benzo[*b*]iodo-3(2*H*)-one **41a** and -Fluoro-1-(3-1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one **41b** were obtained in 1:3 mixture (44.1 mg, 0.128 mmol, overall yield 64%), as a yellow foam. **Rf**: 0.40 (DCM:MeOH 9:1). The two compounds were separated by slow flash column chromatography (EtOAc:MeOH 20:1). *The structure of the obtained regioisomers were assigned by NMR correlation to compound 37.*



4-Fluoro-1-(2-(1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one **41b** (11.1 mg, 32.0 μmol, 16% yield); yellow foam. **Rf**: 0.36 (EtOAc:MeOH 9:1). **IR** ν 3105 (w), 2918 (w), 2851 (w), 1636 (s), 1593 (m), 1564 (w), 1515 (w), 1449 (m), 1422 (w), 1325 (m), 1242 (m), 1112 (m). **¹H NMR** (400 MHz, CDCl₃) δ 7.45 – 7.28 (m, 2H, Ar*H*), 7.07 (dd, *J* = 2.8, 1.6 Hz, 1H, Ar*H*), 6.91 (dd, *J* = 3.9, 1.6 Hz, 1H, Ar*H*), 6.48 (dt, *J* = 7.9, 1.0 Hz, 1H, Ar*H*), 6.42 (dd, *J* = 3.9, 2.8 Hz, 1H, Ar*H*), 3.74 (s, 3H, *NMe*). **¹³C NMR** (101 MHz, CDCl₃) δ 152.6, 134.0, 133.9, 129.9, 125.6, 121.6, 120.7, 120.6, 120.3, 120.0, 112.3, 37.3. **HR-ESI-MS** 345.9730 ([*M*+*H*]⁺, C₁₂H₁₀FINO₂⁺; calc. for 345.9735). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 37.*



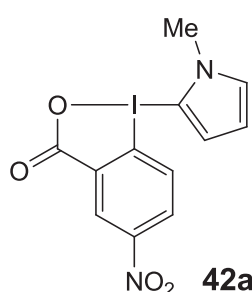
4-Fluoro-1-(3-(1-methyl-1*H*-pyrrole)- 1*H*-1λ₃ -benzo[*b*]iodo-3(2*H*)-one **41a** (33.0 mg, 96.0 μmol, 48% yield); yellow foam. **Rf**: 0.38 (EtOAc:MeOH 9:1). **IR** ν 2919 (m), 2851 (w), 1638 (s), 1612 (s), 1592 (m), 1452 (w), 1339 (w), 1311 (w), 1287 (m), 1233 (w). **¹H NMR** (400 MHz, CDCl₃) δ 7.32 (td, *J* = 8.1, 4.6 Hz, 1H, Ar*H*), 7.27 – 7.22 (m, 2H, Ar*H*), 6.87 – 6.82 (m, 2H, Ar*H*), 6.50 (dd, *J* = 2.9, 1.7 Hz, 1H, Ar*H*), 3.85 (s, 3H, *NMe*). **¹³C NMR** (101 MHz, CDCl₃) δ 164.6 (d, *J* = 266.7 Hz), 163.2, 133.11 (d, *J* = 8.6 Hz), 131.3, 126.2, 121.80 (d, *J* = 12.7 Hz), 121.36 (d, *J* = 3.8 Hz), 119.8, 119.5 (d, *J* = 23.7 Hz), 115.7, 85.9, 37.0. **HR-ESI-MS** 345.9731 ([*M*+*H*]⁺, C₁₂H₁₀FINO₂⁺; calc. for 345.9735). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 37.*

5-Nitro-1-(2-(1-Methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*d*][1,2]iodoxol-3-one (42a) and 5-Nitro-1-(3-(1-methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*d*][1,2]iodoxol-3-one (42b)



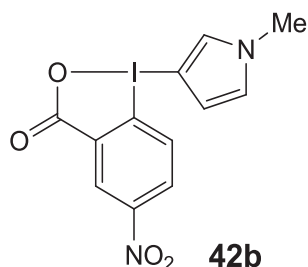
Following procedure **B**: starting from commercially available 1-methyl-1*H*-pyrrole **12** (17.8 μl, 0.200 mmol) and 1-acetoxy-5-nitro-1,2-benziodoxol-3(1*H*)-one **97** (77.0 mg, 0.220 mmol, 1.10 equiv.), after 12 hours 5-nitro-1-(2-(1-methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*d*][1,2]iodoxol-3-one (**42a**) and 5-nitro-

1-(3-1-methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*d*][1,2]iodoxol-3-one (**42b**) were obtained in 4:1 mixture (69.5 mg, 0.187 mmol, overall yield 93%), as a yellow foam. R_f: 0.50 (DCM:MeOH 9:1). The two compounds were separated by slow flash column chromatography (EtOAc:MeOH 20:1). *The structure of the obtained regioisomers were assigned by NMR correlation to compound 37.*



5-nitro-1-(2-1-Methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*d*][1,2]iodoxol-3-one **42a** (54.9 mg, 0.148 mmol, 74% yield); yellow foam. R_f: 0.50 (EtOAc:MeOH 9:1). **NB:** *the reagent is unstable in acidic deuterated solvents and it decompose in short time, we recommend the immediate use after the synthesis. The proton NMR presents about 6% of the open protonated acidic form.* IR ν 3103 (w), 2935 (w), 2925 (w), 2856 (w), 1785 (w), 1716

(m), 1617 (m), 1530 (s), 1459 (w), 1346 (s), 1288 (m), 1250 (m). ¹H NMR (400 MHz, CDCl₃) δ 9.13 (d, *J* = 2.6 Hz, 1H, Ar*H*), 8.27 (dd, *J* = 8.8, 2.5 Hz, 1H, Ar*H*), 7.13 (dd, *J* = 2.8, 1.5 Hz, 1H, Ar*H*), 6.97 (dd, *J* = 4.0, 1.6 Hz, 1H, Ar*H*), 6.82 (d, *J* = 8.9 Hz, 1H, Ar*H*), 6.47 (d, *J* = 1.1 Hz, 1H, Ar*H*), 3.80 (s, 3H, NMe). ¹³C NMR (101 MHz, CDCl₃) δ 164.9, 150.6, 135.6, 130.4, 127.8, 127.0, 126.6, 126.0, 124.8, 112.7, 96.6, 37.5. **HR-ESI-MS** 372.9690 ([M+H]⁺, C₁₂H₁₀IN₂O₄⁺⁺; calc. for 372.9680). *The structure of the obtained regioisomer was assigned by NMR correlation to compound 37.*



5-nitro-1-(3-1-Methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*d*][1,2]iodoxol-3-one **42b** (14.6 mg, 0.039 mmol, 19% yield); yellow foam. R_f: 0.46 (EtOAc:MeOH 9:1). **NB:** *the reagent is unstable in acidic deuterated solvents and it decompose in short time, we recommend the immediate use after the synthesis. The proton and carbon NMRs present about 8% of the open protonated acidic form.* IR ν 3092 (w), 2957 (w), 2928

(w), 1716 (m), 1623 (m), 1529 (s), 1346 (s), 1303 (w), 1109 (w), 1076 (w). ¹H NMR (400 MHz, CDCl₃) δ 9.18 (d, *J* = 2.6 Hz, 1H, Ar*H*), 8.24 (dd, *J* = 8.9, 2.7 Hz, 1H, Ar*H*), 7.23 (t, *J* = 1.9 Hz, 1H, Ar*H*), 7.20 (d, *J* = 8.9 Hz, 1H, Ar*H*), 6.90 (m, 1H, Ar*H*), 6.56 (dd, *J* = 2.9, 1.7 Hz, 1H, Ar*H*), 3.89 (s, 3H, NMe). ¹³C NMR (101 MHz, CDCl₃) δ 194.4, 150.5, 135.6, 131.3, 127.1, 126.8, 126.7, 126.6, 122.3, 115.8, 84.2, 37.2. **HR-ESI-MS** 372.9691 ([M+H]⁺, C₁₂H₁₀IN₂O₄⁺⁺; calc. for

372.9680). The structure of the obtained regioisomer was assigned by NMR correlation to compound **37**.

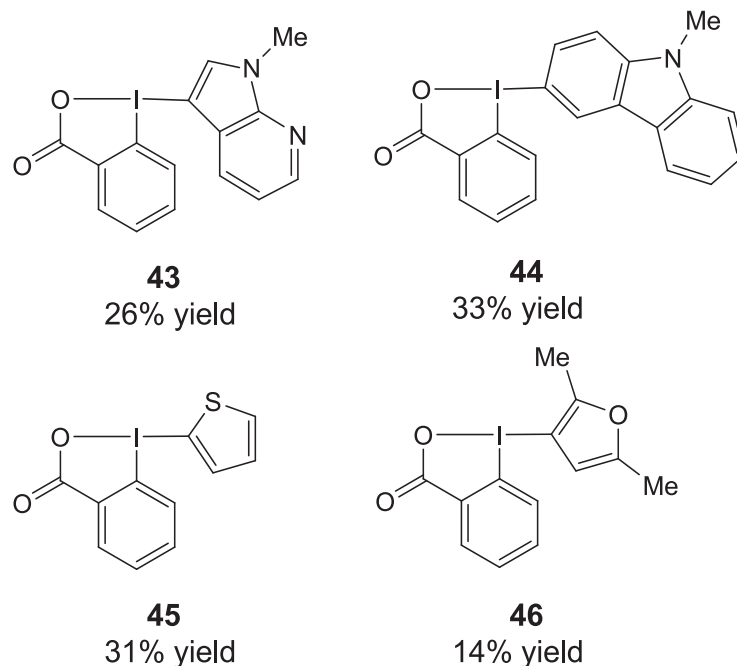
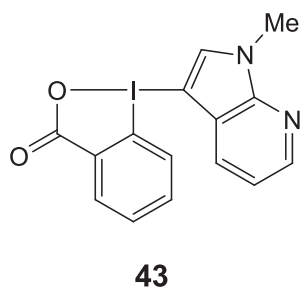


Figure S7: Scope of Heterocyclic-BX reagents (6)

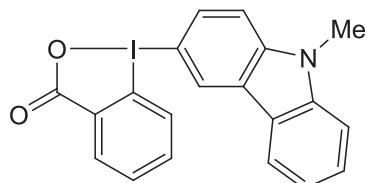
1-(3-(1-Methyl-1H-pyrrolo[2,3-b]pyridine)-1H-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one (**43**)



Following procedure A: starting from commercially available 1-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (132 mg, 1.00 mmol), after 16 hours 1-(3-(1-methyl-1*H*-pyrrolo[2,3-*b*]pyridine)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **43** (114 mg, 0.301 mmol, 30% yield) was obtained as a brown amorphous solid. **Rf**: 0.2 (DCM:MeOH 9:1). **IR** ν 2925 (w), 2852 (w), 1719 (s), 1599 (m), 1585 (m), 1468 (m), 1408 (w), 1348 (w), 1289 (m), 1262 (s), 1136 (m), 1103 (w), 1042 (w), 1017 (m), 976 (w). **¹H NMR** (400 MHz, CD₂Cl₂) δ 8.37 (dd, *J* = 4.7, 1.6 Hz, 1H, Ar*H*), 8.06 (dd, *J* = 7.9, 1.2 Hz, 1H, Ar*H*), 7.96 (dd, *J* = 7.9, 1.7 Hz, 1H, Ar*H*), 7.92 (dd, *J* = 7.9, 1.7 Hz, 1H, Ar*H*), 7.46 (td, *J* = 7.7, 1.2 Hz, 1H, Ar*H*), 7.25 – 7.19 (m, 2H, Ar*H*), 7.14 (dd, *J* = 7.9, 4.7 Hz, 1H, Ar*H*), 3.86 (s, 3H, CH₃N). **¹³C NMR** (101 MHz, CD₂Cl₂) δ 168.6, 144.4, 142.3, 134.3, 133.8, 132.1, 128.7, 127.0, 126.3, 118.8, 116.5, 103.2, 94.9, 31.7 (one Carbon

signal not resolved). **HR-ESI-MS** 378.9945 ($[M+H]^+$, $C_{15}H_{12}IN_2O_2^+$; calc. for 378.9938). The structure of the obtained regioisomer was assigned by NMR correlation to compound **9b**.

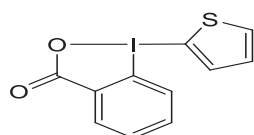
1-(3-9-Methyl-9H-carbazole)-1H-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one (**44**)



44

Following procedure **A**: starting from commercially available 9-methyl-9*H*-carbazole (181 mg, 1.00 mmol), after 16 hours 1-(3-9-methyl-9*H*-carbazole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **9m** (110 mg, 0.257 mmol, 33% yield) was obtained as a grey amorphous solid. **Rf**: 0.2 (DCM:MeOH 9:1). **IR** ν 3082 (w), 2974 (w), 2924 (w), 2816 (w), 1652 (s), 1588 (w), 1570 (w), 1456 (w), 1440 (m), 1295 (m), 1245 (w), 1139 (w), 1017 (w), 982 (m), 831 (w). **¹H NMR** (400 MHz, $CDCl_3$) δ 8.67 (d, J = 1.6 Hz, 1H, Ar*H*), 8.47 (dd, J = 7.5, 1.7 Hz, 1H, Ar*H*), 8.14 (d, J = 7.9 Hz, 1H, Ar*H*), 7.96 (dd, J = 8.5, 1.6 Hz, 1H, Ar*H*), 7.63 (ddd, J = 8.4, 7.1, 1.2 Hz, 1H, Ar*H*), 7.59 (d, J = 8.5 Hz, 1H, Ar*H*), 7.57 – 7.52 (m, 2H, Ar*H*), 7.37 (td, J = 7.5, 1.2 Hz, 1H, Ar*H*), 7.30 (ddd, J = 8.5, 7.1, 1.7 Hz, 1H, Ar*H*), 6.69 (dd, J = 8.5, 0.9 Hz, 1H, Ar*H*), 3.98 (s, 3H, NCH_3). **¹³C NMR** (101 MHz, $CDCl_3$) δ 166.5, 142.4, 141.4, 133.4, 133.3, 132.7, 130.6, 130.0, 127.7, 125.8, 125.7, 121.4, 120.8, 120.7, 116.3, 112.0, 109.3, 101.8, 53.4, 29.5. **HR-ESI-MS** 428.0147 ($[M+H]^+$, $C_{20}H_{15}INO_2^+$; calc. for 428.0142).

1-(2-1*H*-Thiophene)-1H-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one (**45**)

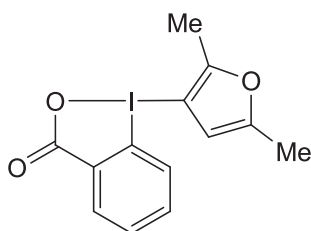


45

Following procedure **A**: starting from commercially available thiophene (80.0 μ L, 1.00 mmol) and using $Sc(OTf)_3$ as the Lewis Acid (20 mol%), after 16 hours 1-(2-1*H*-thiophene)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one (**45**) (102 mg, 0.309 mmol, 31% yield) was obtained as a light yellow amorphous solid. **NB: the reagent is unstable in protic deuterated solvents and it decompose in short time, we recommend the immediate use after the synthesis. The proton NMR presents about 7% of the open protonated form.** **Rf**: 0.4 (DCM:MeOH 9:1). **IR** ν 3080 (w), 2958 (w), 2925 (m), 2853 (w), 1716 (w), 1622 (s), 1603 (s), 1558 (m), 1438 (w), 1354 (w), 1341 (w), 1299 (w), 1223 (w), 1006 (w), 951 (w), 834 (w), 830 (w). **¹H NMR** (400 MHz, CD_3OD) δ 8.28 (dd, J = 7.5, 1.7 Hz, 1H, Ar*H*), 8.05 (dd, J = 5.2, 1.2 Hz, 1H, Ar*H*), 7.98 (dd, J =

3.7, 1.2 Hz, 1H, *ArH*), 7.70 (td, *J* = 7.4, 0.9 Hz, 1H, *ArH*), 7.61 (ddd, *J* = 8.7, 7.2, 1.7 Hz, 1H, *ArH*), 7.37 (dd, *J* = 5.3, 3.6 Hz, 1H, *ArH*), 6.92 (dd, *J* = 8.3, 0.9 Hz, 1H, *ArH*). ¹³C NMR (101 MHz, CDCl₃) δ 166.6, 141.5, 137.1, 134.1, 132.7, 131.0, 130.4, 125.2, 117.8, 104.2 (one aromatic Carbon signal not resolved). **HR-ESI-MS** 330.9291 ([*M*+*H*]⁺, C₁₁H₈IO₂S⁺; calc. for 330.9284).

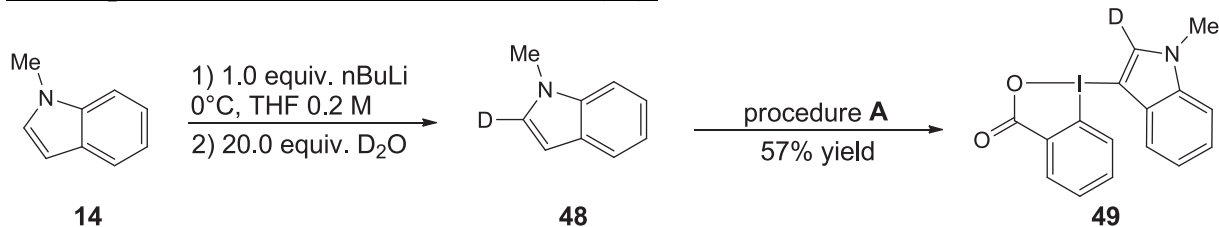
1-(3-1*H*-2,5-dimethylfuran)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (46)



46

Following procedure **A**: starting from commercially available 2,5-dimethylfuran (107 μL, 1.00 mmol) and using In(OTf)₃ as the Lewis Acid (20 mol%), after 24 hours 1-(3-1*H*-2,5-dimethylfuran)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (**9t**) (47.0 mg, 0.137 mmol, 14% yield) was obtained as a brown resin. **Rf**: 0.3 (DCM:MeOH 9:1). **IR** ν 3430 (w), 3111 (w), 3065 (w), 2923 (w), 2854 (w), 1607 (s), 1559 (m), 1438 (m), 1348 (m), 1298 (w), 1229 (w), 1128 (w), 1039 (w), 1007 (w), 926 (w), 831 (m). ¹H NMR (400 MHz, CDCl₃) δ 8.28 (dd, *J* = 7.4, 1.8 Hz, 1H, *ArH*), 7.50 (t, *J* = 7.3 Hz, 1H, *ArH*), 7.43 (td, *J* = 7.7, 7.3, 1.8 Hz, 1H, *ArH*), 7.00 (d, *J* = 8.1 Hz, 1H, *ArH*), 6.21 (s, 1H, *ArH*), 2.42 (s, 3H, *FuraneCH*₃), 2.31 (s, 3H, *FuraneCH*₃). ¹³C NMR (101 MHz, CDCl₃) δ 166.9, 158.9, 154.2, 133.5, 133.1, 132.4, 130.4, 125.4, 115.0, 110.4, 88.0, 13.4, 13.2. **HR-ESI-MS** 342.9827 ([*M*+*H*]⁺, C₁₃H₁₂IO₃⁺; calc. for 342.9826).

2.6 Preparation of Deuterated IndoleBX (49).

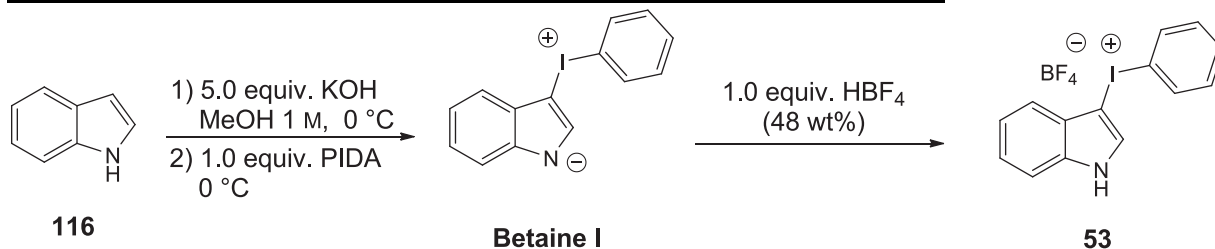


Following a reported procedure,^[19] a flame dried flask is charged with freshly distilled 1-methyl-1*H*-indole **14** (0.374 mL, 3.00 mmol) and then flushed with argon. Anhydrous THF (9 mL, 0.3 M) is added, and the reaction is allowed to stir until all the 1-methylindole is dissolved. The solution is cooled to 0 °C, and *n*BuLi 2.5 M (1.80 mL, 4.50 mmol, 1.5 equiv.) is added dropwise. The resulting solution is allowed to warm to ambient temperature, and allowed to stir for an additional 20 minutes. Then, D₂O (1.20 mL, 60.0 mmol, 20.0 equiv.) is added dropwise. After the solution is fully quenched with D₂O, it is extracted with hexane (5x3 mL). Then the organic phase is dried

over Na₂SO₄ and the solvent is removed *in vacuo*. The final product **48** was purified by distillation from molecular sieves. The product **was 88 % enriched** with deuterium in the 2-position, as determined by ¹H NMR.

Following general procedure A, 1-(2-*D*-1-methylindole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **49** (215 mg, 0.569 mmol, 56.9 % yield) is obtained as a slightly brown foam. The product **was 88 % enriched** with deuterium in the 2-position, as determined by ¹H NMR. **Rf**: 0.28 (DCM:MeOH 9:1). **IR** ν 3057 (w), 2945 (w), 2326 (w), 1601 (s), 1555 (m), 1474 (m), 1415 (m), 1359 (m), 1277 (m), 1262 (m), 1157 (w), 1032 (m), 899 (m), 832 (m). **¹H NMR** (400 MHz, CDCl₃:AcOH 10:1) δ 8.22 (dd, *J* = 7.5, 1.7 Hz, 1H, Ar*H*), 8.02 (s, 0.12H, CH + CD), 7.48 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.40 – 7.33 (m, 2H, Ar*H*), 7.32 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.22 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.18 (ddd, *J* = 8.6, 5.8, 2.3 Hz, 1H, Ar*H*), 6.76 (d, *J* = 8.3 Hz, 1H, Ar*H*), 4.00 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 167.3, 139.3 (m, C-*D*), 137.4, 133.2, 133.0, 132.1, 130.2, 129.1, 125.5, 123.9, 122.3, 119.5, 115.8, 110.7, 77.3, 33.8. **HR-ESI-MS** 378.9989 ([M+H]⁺, C₁₆H₁₃INO₂⁺; calc. for 378.9987).

2.7 Preparation of β-Phenyliodonioindole Tetrafluoroborate (**53**).

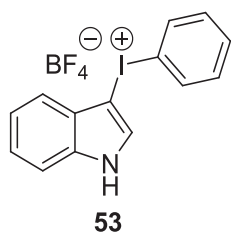


Following a reported procedure,^[20] to a stirred solution of fine crushed KOH (5.61 g, 100 mmol, 5.00 equiv.) in MeOH (20.0 mL, 1.0 M), 1*H*-indole **116** (2.34 g, 20.0 mmol, 1.00 equiv.) was added in portions at 0 °C. The resulting mixture was left stirring at 0 °C until complete dissolution of the 1*H*-indole (1.5 h). Then PIDA (6.44 g, 20.0 mmol, 1.00 equiv.) was added portionwise and the reaction mixture left stirring at 0 °C for 1.5 h. **Betaine I** intermediate (dark yellow green solid in suspension) was then removed by filtration over a glass-synthered funnel, washed with cold MeOH and CHCl₃ and air dried in the dark at 0 °C. **Betaine I** intermediate (2.20 g, 6.89 mmol, 35% yield) was obtained as a dark yellow green amorphous solid.

Caution: *Betaine I is a highly unstable intermediate, it is reported to detonate at room temperature; do NOT grind it, it may explode. The Betaine I intermediate decomposes at -20 °C, it is recommended to be used immediately after its preparation.*

HB F_4 (450 μL , 6.89 mmol, 1.00 equiv., 48 wt.% solution in H_2O) was added to EtOH (10 mL) and the resulting solution cooled at -15 °C; then **Betaine I** intermediate (2.20 g, 6.89 mmol, 1.00 equiv.) was added portionwise under vigorous stirring at -15 °C. After all of **Betaine I** had been added, the dark brown resulting reaction mixture was diluted with Et $_2$ O (50 mL) and stirred for 1.5 h at -15 °C. Then stirring was stopped and the reaction left at -15 °C for 30 min. The resulting precipitate was then removed by filtration over a glass-synthered funnel and dried at 0 °C to give β -Phenyliodonioindole Tetrafluoroborate **53** (2.10 g, 5.16 mmol, 75% yield) as a yellowish green amorphous solid.

Caution: *β -Phenyliodonioindole Tetrafluoroborate 53 is an unstable salt and it was immediately used after its preparation.*



IR ν 3375 (s), 3132 (w), 1561 (m), 1491 (m), 1472 (s), 1411 (s), 1340 (m), 1328 (m), 1279 (s), 1244 (s). **^1H NMR** (400 MHz, DMSO- d_6) δ 12.32 (brs, 1H, NH), 8.40 (d, J = 2.7 Hz, 1H, ArH), 8.14 – 8.12 (m, 2H, ArH), 7.74 (m, 1H, ArH), 7.58 – 7.55 (m, 2H), 7.47 – 7.43 (m, 2H), 7.35 – 7.16 (m, 2H). (presence of Et $_2$ O residual solvent as the NMR analysis was performed on the slightly wet compound to prevent decomposition). **^{13}C NMR** (101 MHz, DMSO- d_6) δ 135.8, 135.1, 134.0, 131.5, 127.1, 123.6, 121.9, 118.8, 117.3, 113.0, 78.0. (one aromatic Carbon signal not resolved). **HR-ESI-MS** 319.9932 ($[\text{M}^+]$, $\text{C}_{14}\text{H}_{11}\text{IN}$; calc. for 319.9931).

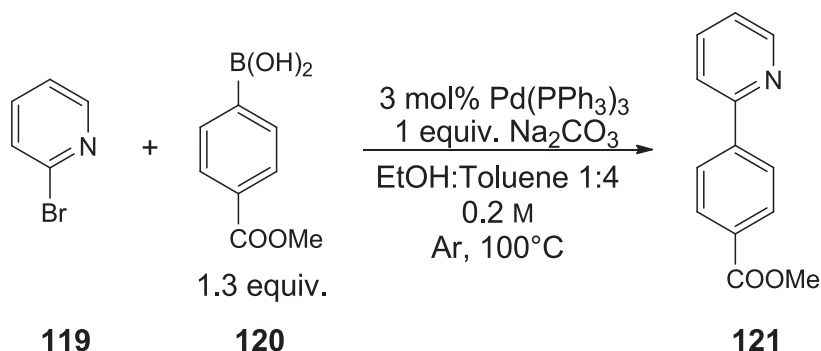
3. Rh-Catalyzed C-H Indolization of Arenes *via* C-H activation.

All commercially available chemicals were purchased from the suppliers quoted in Paragraph 1.0 of Supplementary Informations: these chemicals were purified through a short plug of celite prior to their use in catalysis. The synthesis of non commercial available compounds is presented below.

The synthesis of the starting materials **121**, **123**, **127** the optimization process of compound **52** and products **52**, **54-75** had been already described before.^[1] The procedures here reported are taken from the cited publication to facilitate reproduction of the results by having all the data in the same file.

3.1 Synthesis of Starting Materials.

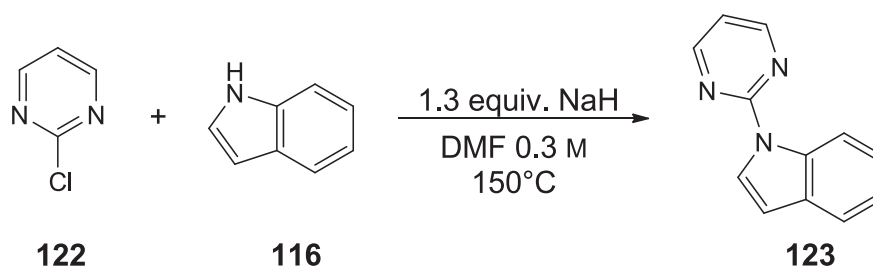
Methyl 4-(pyridin-2-yl)benzoate (**44**)



Following a reported procedure,^[21] to a solution of commercially available 2-bromopyridine **119** (100 μ L, 1.00 mmol) in a mixture of 4/1 toluene/EtOH (5 mL, 0.2 M) was added Na₂CO₃ (106 mg, 1.00 mmol, 1.00 equiv.) followed by Pd(PPh₃)₄ (34.7 mg, 30.0 μ mol, 3 mol %) and (4-(methoxycarbonyl)phenyl)boronic acid **120** (234 mg, 1.30 mmol, 1.30 equiv.) under argon atmosphere in a 50 mL two-necked flask. The reaction mixture was refluxed for 12 h, and then cooled to room temperature. To the reaction mixture was added sat. aqueous NH₄Cl (15 mL), then the mixture was extracted by EtOAc (3x5 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated *in vacuo*. The resulting crude product was purified by flash chromatography (Pentane:EtOAc 4:1) to afford methyl 4-(pyridin-2-yl)benzoate **121** (181 mg, 0.849 mmol, 85% yield) as a white solid. IR ν 2944 (w), 2848 (w), 1708 (s), 1606 (w), 1586 (m),

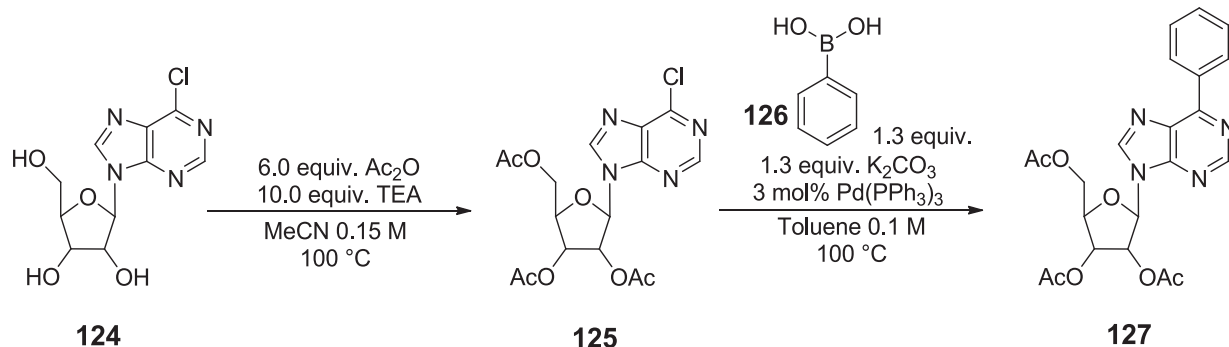
1466 (w), 1435 (m), 1405 (w), 1319 (w), 1274 (s), 1194 (m), 1183 (m), 1153 (w), 1111 (s), 1014 (m), 965 (m), 868 (w), 830 (w), 797 (w), 754 (vs), 699 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.64 (d, *J* = 4.7 Hz, 1H, Ar*H*), 8.06 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.98 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.73 – 7.63 (m, 2H, Ar*H*), 7.19 (q, *J* = 4.6 Hz, 1H, Ar*H*), 3.85 (s, 3H COOMe). **¹³C NMR** (101 MHz, CDCl₃) δ 166.8, 156.1, 149.8, 143.4, 136.8, 130.3, 130.0, 126.7, 122.8, 120.9, 52.1. NMR values are in accordance with the data reported in literature.^[20]

1-(Pyrimidin-2-yl)-1*H*-indole (**123**)



Following a reported procedure,^[22] commercially available 1*H*-indole **116** (586 mg, 5.00 mmol) was dissolved in N,N-dimethylformamide (15.0 mL, 0.3M) and sodium hydride (60% suspension in mineral oil, 300 mg, 7.50 mmol, 1.50 equiv.) was added at r.t. and the reaction mixture was stirred for one hour. Upon seizing of gas release, commercially available 2-chloropyrimidine **122** (573 mg, 5.00 mmol, 1.00 equiv.) was added portionwise. The reaction was heated up to 150 °C and stirred overnight. After 10 hours the reaction was allowed cooling to r.t. and was then quenched with water (20 mL). The majority of the solvent was removed under reduced pressure, then the crude was diluted with Et₂O (25 mL), the organic layer washed with brine (3x10 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. Flash column chromatography (Pentane:EtOAc 4:1) afforded 1-(pyrimidin-2-yl)-1*H*-indole **123** (926 mg, 4.74 mmol, 95% yield) as a light brown oil. **IR** ν 3138 (w), 3108 (w), 1575 (s), 1525 (m), 1456 (s), 1309 (m), 1204 (s), 1080 (m), 970 (s), 776 (m), 750 (w), 731 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.94 (d, *J* = 8.4 Hz, 1H, Ar*H*), 8.75 (d, *J* = 4.8 Hz, 2H, Ar*H*), 8.40 (d, *J* = 3.7 Hz, 1H, Ar*H*), 7.75 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.51 – 7.43 (m, 1H, Ar*H*), 7.37 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.07 (t, *J* = 4.8 Hz, 1H, Ar*H*), 6.83 (d, *J* = 3.6 Hz, 1H, Ar*H*). **¹³C NMR** (101 MHz, CDCl₃) δ 157.7, 157.4, 135.1, 131.1, 125.6, 123.4, 121.9, 120.6, 116.2, 115.8, 106.6. NMR values are in accordance with the data reported in literature.^[23]

(2*R*,3*R*,4*R*,5*R*)-2-(Acetoxymethyl)-5-(6-phenyl-9*H*-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate (50**)**



Following a reported procedure,^[24] commercially available (2*R*,3*R*,4*S*,5*R*)-2-(6-chloro-9*H*-purin-9-yl)-5-(hydroxymethyl)tetrahydrofuran-3,4-diol **47** (573 mg, 2.00 mmol, 1.00 equiv.) was suspended in MeCN (12.5 mL, 0.15 M). Then Triethylamine (2.90 mL, 20.0 mmol, 10.0 equiv.) and Acetic Anhydride (1.10 mL μ l, 12.00 mmol, 6.00 equiv.) were added at 0° C. After stirring for 1h at room temperature, the mixture was refluxed for 5 hours. The resulting solution was evaporated to dryness and EtOAc (30 mL) and water (30 mL) were added. The organic layer was separated, dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a light brown oil, which was recrystallized from EtOAc/Ether to give (2*R*,3*R*,4*R*,5*R*)-2-(acetoxymethyl)-5-(6-chloro-9*H*-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate **48** (693 mg, 1.68 mmol, 84 % yield)

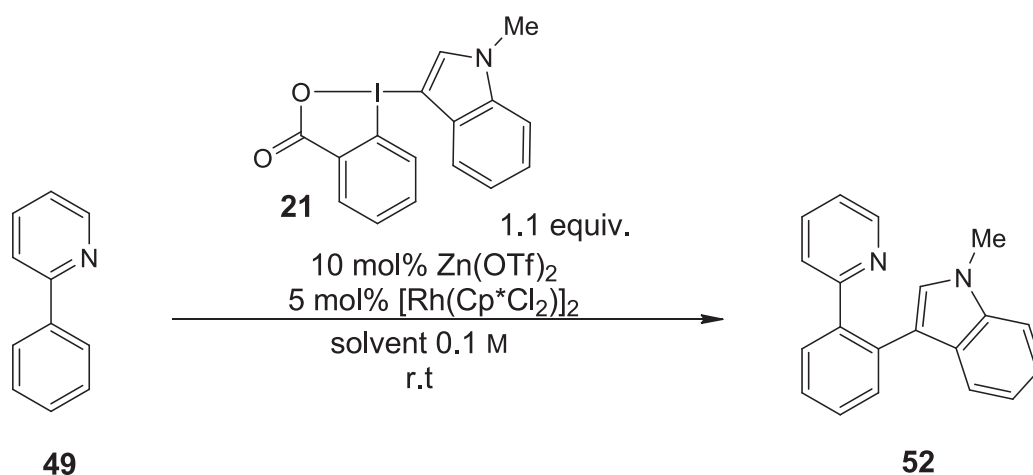
Subsequently, to a solution of (2*R*,3*R*,4*R*,5*R*)-2-(acetoxymethyl)-5-(6-chloro-9*H*-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate **48** (500 mg, 1.21 mmol) in a mixture of 4/1 toluene (12 mL, 0.1 M) was added K₂CO₃ (218 mg, 1.58 mmol, 1.30 equiv.) followed by Pd(PPh₃)₄ (42.0 mg, 30.0 μ mol, 3 mol %) and phenylboronic acid **49** (192 mg, 1.58 mmol, 1.30 equiv.) under argon atmosphere in a 20 mL two-necked flask. The reaction mixture was refluxed for 12 h, and then cooled to room temperature. To the reaction mixture was added sat. aqueous NH₄Cl (15 mL), then the mixture was extracted by EtOAc (3x5 mL). The combined organic extracts were dried over MgSO₄, filtered and concentrated *in vacuo*. The resulting crude product was purified by flash chromatography (Pentane:EtOAc 4:1) to afford (2*R*,3*R*,4*R*,5*R*)-2-(acetoxymethyl)-5-(6-phenyl-9*H*-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate **50** (523 mg, 1.15 mmol, 95% yield) as a white

solid. **IR** ν 2926 (m), 1749 (s), 1583 (s), 1566 (s), 1439 (m), 1220 (s), 1101 (m), 766 (m), 693 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.95 (s, 1H, ArH), 8.68 (dd, J = 8.0, 1.8 Hz, ArH), 8.21 (s, 1H, ArH), 7.52 – 7.43 (m, 3H, ArH), 6.22 (d, J = 5.3 Hz, 1H, CH), 5.95 (t, J = 5.4 Hz, 1H, CH), 5.64 (m, 1H, CH), 4.45 – 4.24 (m, 3H, CH + CH₂), 2.08 (s, 3H, CH₃), 2.05 (s, 3H, CH₃), 2.00 (s, 3H, CH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 169.9, 169.2, 169.0, 154.7, 152.1, 151.6, 142.5, 135.0, 131.2, 130.7, 129.4, 128.2, 86.1, 79.9, 72.7, 70.2, 62.7, 20.3, 20.1, 20.0. NMR values are in accordance with the data reported in literature.^[23]

3.2 Optimization of the Rh-Catalyzed Indolization of Arenes *via* C-H activation.

In a vial, 2-phenylpyridine **49** (14.0 μ l, 0.100 mmol), 1-(3-(1-methyl-1*H*-indole)-1*H*-1*λ*₃ - benzo[*b*]iodo-3(2*H*)-one **21** (1.10 equiv.), the catalyst system (1.25-5 mol%) and the relative additive (2.5-20 mol%) were dissolved in the appropriate dry solvent (0.1 M) under nitrogen. The reaction mixture was degassed (freeze-thaw-pump) and then stirred at the reported T in °C overnight. The reaction mixture was then allowed to cool to r.t., the organic layer was washed with sat. aqueous NaHCO₃ (2 mL), and the solvent was removed under reduced pressure. Flash column chromatography (Pentane:EtOAc 4:1) afforded the desired product **52** (*see compound 52's characterization for all the chemical data*).

Table S3: Screening of solvents

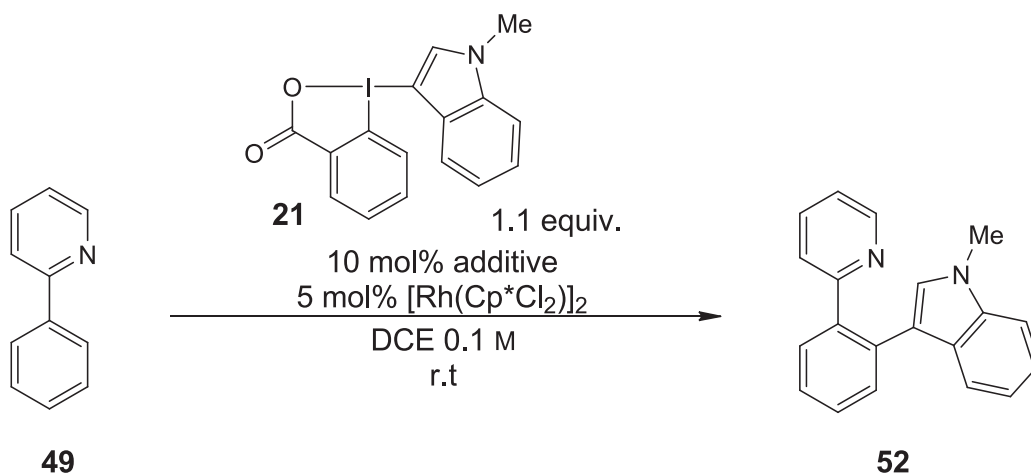


Entry	Solvent	Yield% ^a
1	DCM	25%

2	DCE	55%
3	MeOH	-
4	EtOH	-
5	TFE	16%
6	Chlorobenzene	-
7	1,2-Chlorobenzene	-
8	Toluene	-
9	DMF (110°C)	66%

a) Substrate **49** (0.100 mmol), IndoleBX **21** (0.110 mmol), $[\text{Rh}(\text{Cp}^*\text{Cl}_2)]_2$ (5 mol%), $\text{Zn}(\text{OTf})_2$ (10 mol%) and solvent (0.1 M) at 25 °C. Isolated yield after flash chromatography is given.

Table S4: Screening of additives

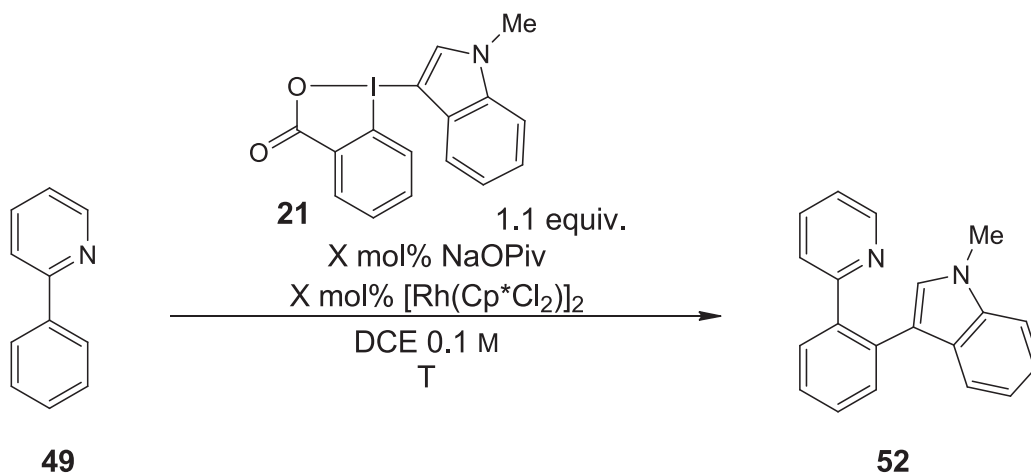


Entry	Additive	Yield% ^a
1	-	-
2	$\text{Zn}(\text{OTf})_2$	55% ^b
3	$\text{Sc}(\text{OTf})_3$	56% ^c
4	K_2CO_3	28%
5	$\text{Zn}(\text{NTf}_2)_2$	56%
6	AgNTf_2	-
7	$\text{AgSbF}_6^{\text{d}}$	17%

8	NaOAc	69%
9	KOAc	37%
10	NaOPiv	72%
11	KOPiv	49%
12	CsOPiv	36%

a) Substrate **49** (0.100 mmol), IndoleBX **21** (0.110 mmol), [Rh(Cp*Cl₂)₂] (5 mol%), **additive** (10 mol%) and DCE (0.1 M) at 25 °C. Isolated yield after flash chromatography is given. b) incomplete conversion, remaining starting material completely recovered. c) decomposition observed. d) T of the reaction is 50°C.

Table S5: Screening of the catalyst:additive ratio at different T°C.



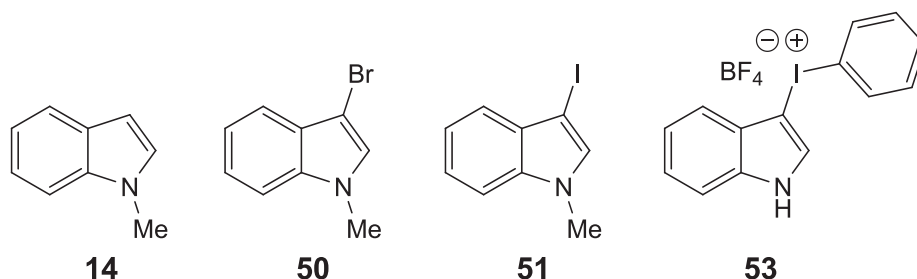
Entry	Catalyst (mol%)	Additive (mol%)	T°C	Yield% ^a
1	[Rh(Cp*Cl ₂) ₂] (1.25)/AgSbF ₆ (2.5)	NaOPiv (2.5)	r.t.	traces ^b
2	[Rh(Cp*Cl ₂) ₂] (1.25)/AgSbF ₆ (10)	NaOPiv (10)	r.t.	traces ^b
3	[Rh(Cp*Cl ₂) ₂] (1.25)/AgSbF ₆ (10)	NaOPiv (10)	40°C	traces ^b
4	[Rh(Cp*Cl ₂) ₂] (1.25)/AgSbF ₆ (10)	NaOPiv (10)	50°C	37% ^b

5	$[\text{Rh}(\text{Cp}^*\text{Cl}_2)_2]$ (2.5)/AgSbF ₆ (5)	NaOPiv (5)	r.t.	traces ^c
6	$[\text{Rh}(\text{Cp}^*\text{Cl}_2)_2]$ (2.5)/AgSbF ₆ (10)	NaOPiv (10)	r.t.	78%
7	$[\text{Rh}(\text{Cp}^*\text{Cl}_2)_2]$ (2.5)/AgSbF ₆ (10)	NaOPiv (10)	50°C	82%
8	$[\text{Rh}(\text{Cp}^*\text{Cl}_2)_2]$ (2.5)/AgSbF₆ (10)	NaOPiv (10)	80°C	85%
9	$[\text{Rh}(\text{Cp}^*\text{Cl}_2)_2]$ (5)/AgSbF ₆ (10)	NaOPiv (10)	r.t.	90%

a) Substrate **49** (0.100 mmol), IndoleBX **21** (0.110 mmol), $[\text{Rh}(\text{Cp}^*\text{Cl}_2)_2]$ (**X** mol%), NaOPiv (**X** mol%) and DCE (0.1 M) at 25 °C. Isolated yield after flash chromatography is given. b) the reaction time was 48 hours, hypervalent iodine decomposition was observed.

3.3 Control experiments for the Indolization of Arenes via C-H activation.

In order to assess the superiority of our reagents in catalysis compared to other indole-transfer reagents already known in cross-coupling reactions, we tested the latter under different sets of conditions. Substrates **14**, **50** and **51** are commercially available, while compound **53** needed to be prepared and immediately used in the catalytic process.

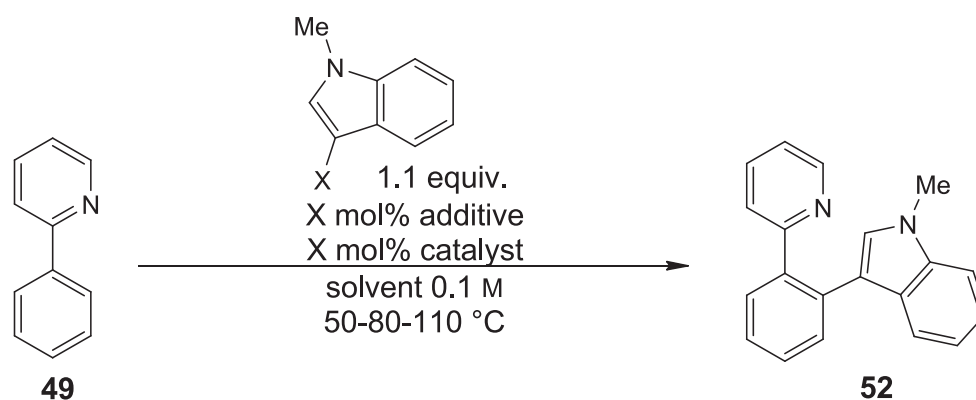


Substrates **50**, **51** and **53** were tested under our optimized conditions (*table S6, entries 1-3*) at different temperatures (r.t.-50-60-110 °C): no conversion was observed. The hypervalent indolinium salt **53** was also tested in presence of NaSbF₆ (*table S6, entry 4*) as an alternative salt to promote the exchange of BF₄⁻ counteranion with SbF₆⁻, but no conversion was observed. Substrates **50** and **51** were then tested under established conditions for Pd-catalyzed cross couplings of C3-halogenated indoles. 3- Bromo-N-methylindole **50** was tested under Hartwig Pd-catalyzed amination conditions^[25] (*table S6, entry 5*), carbonylative Sonogashira conditions^[26] (*table S6,*

entry 6) and Heck conditions^[27] (table S6, entry 7): the desired product was never observed. Furthermore, when 3-Iodo-*N*-methylindole **51** was tested under Suzuki and Sonogashira cross coupling conditions^[28] (table S6, entries 8-9) no product was detected.

In Table S7 oxidative methods were examined (table S7, entries 1,4),^[29] Shi conditions (table S7, entries 2,5),^[30] and Fagnou conditions (table S7, entries 3,6);^[31] the desired compound was never observed.

Table S6: Control experiments (I)

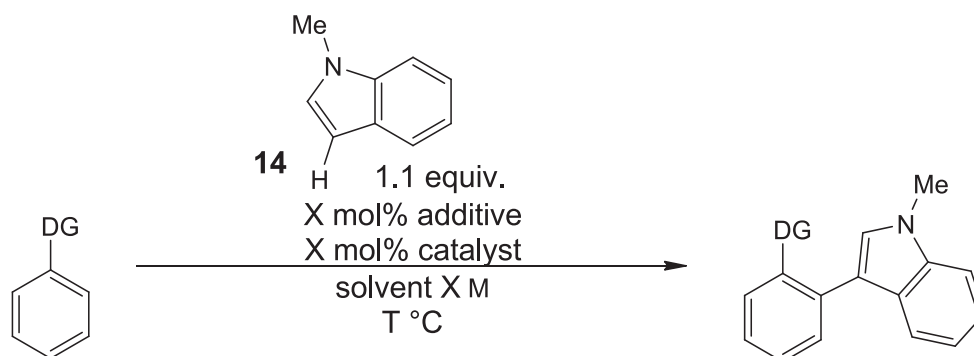


Entry	X	Catalyst (mol%)	Additive (mol%)	Solvent (M)	Yield% ^a
1	H (14)	[Rh(Cp*Cl ₂) ₂] (2.5)/AgSbF ₆ (10)	NaOPiv (10)	DCE (0.1 M)	-
2	I (51)	[Rh(Cp*Cl ₂) ₂] (2.5)/AgSbF ₆ (10)	NaOPiv (10)	DCE (0.1 M)	-
3	I ^(III) (53)	[Rh(Cp*Cl ₂) ₂] (2.5)/NaSbF ₆ (10)	NaOPiv (10)	DCE (0.1 M)	-
4	I ^(III) (53)	[Rh(Cp*Cl ₂) ₂] (2.5)/AgSbF ₆ (10)	NaOPiv (10)	DCE (0.1 M)	-
5	Br (50)	Pd(dba) ₂ (5)/ PPh ₃ (5)	-	Toluene (0.2 M)	-
6	Br (50)	PdCl ₂ (5)/ XanthPhos (5)	TEA (3 equiv.)	Dioxane (0.2 M)	-

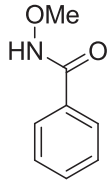

7	Br (50)	Pd(OAc) ₂ (20)/ P(<i>o</i> -Tol) ₃ (20)	TEA (3 equiv.)	Toluene (0.2 M)	-
8	I (51)	PdCl ₂ PPh ₃ (5)	CuI (10)/ TEA (3 equiv.)	DMF (0.1 M)	-
9	I (51)	Pd(PPh ₃) ₃ (2.5)	Na ₂ CO ₃ (1 equiv.)	DMF (0.1 M)	-

a) Substrate **49** (0.100 mmol), Indole source (0.110 mmol), Catalyst (**X** mol%), Additive (**X** mol%) and Solvent (0.1 M) at 50°-80°-110°C.T

Table S7: Control experiments (II)



Entry	Substrate	Equiv.	Equiv. 8a	Catalyst (mol%)	Additive (mol%)	Solvent (M)/ T °C	Yield% ^a
1		1	20	[Rh(Cp*Cl ₂) ₂] (2.5)/CsOPiv(20)	PivOH (50) 2.0 equiv. C ₆ Br ₆ /2.2 equiv. Cu(OAc) ₂	2Cl- <i>p</i> -xylene (0.33 M)/140 °C	-
2		1	6.0	Pd(OAc) ₂ (10)	Cu(OTf) ₂ (20) O ₂ 1 atm.	EtCOOH (0.2 M)/120°C	-
3		60	1	Pd(TFA) ₂ (5)	3.0 equiv. Cu(OAc) ₂ /6.0 equiv. PivOH	neat in arene (0.15 M)	-
4		1	20	[Rh(Cp*Cl ₂) ₂] (2.5)/CsOPiv(20)	PivOH (50) 2.0 equiv. C ₆ Br ₆ /2.2 equiv. Cu(OAc) ₂	2Cl- <i>p</i> -xylene (0.33 M)/140 °C	-

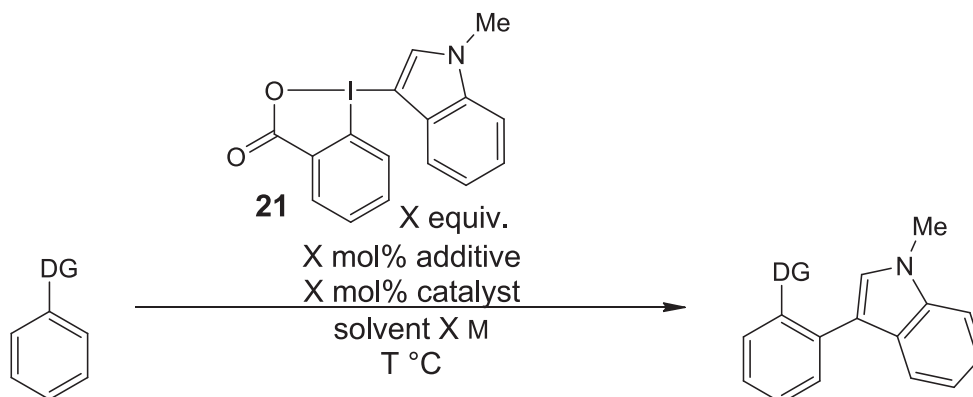
5		1	6.0	Pd(OAc) ₂ (10)	Cu(OTf) ₂ (20) O ₂ 1 atm.	EtCOOH (0.2 M)/120 °C	-
6		60	1	Pd(TFA) ₂ (5)	3.0 equiv. Cu(OAc) ₂ /6.0 equiv. PivOH	neat in arene (0.15 M)/110 °C	-

78

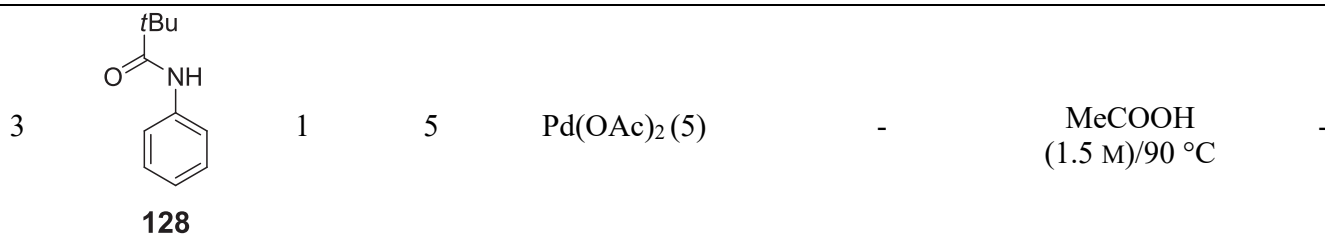
a) Reaction performed on 0.1 mmol of the limiting reagent; substrate (**X** mmol), Indole **14** (**X** mmol), Catalyst (**X** mol%), Additive (**X** mol%) and Solvent (**X** M) at T °C.

Finally, in *Table S8* are reported control experiments employing conditions suitable for hypervalent iodine reagents such as Kita conditions (*table S8, entry 1*),^[32] Sanford conditions (*table S8, entry 2*),^[33] and Daugulis conditions (*table S8, entry 3*);^[34] the desired compounds was not observed also in this case; All conditions screened in *Tables S6, S7* and *S8* failed to afford the desired product, thus demonstrating the unique reactivity of our reagents.

Table S8: Control experiments (III)



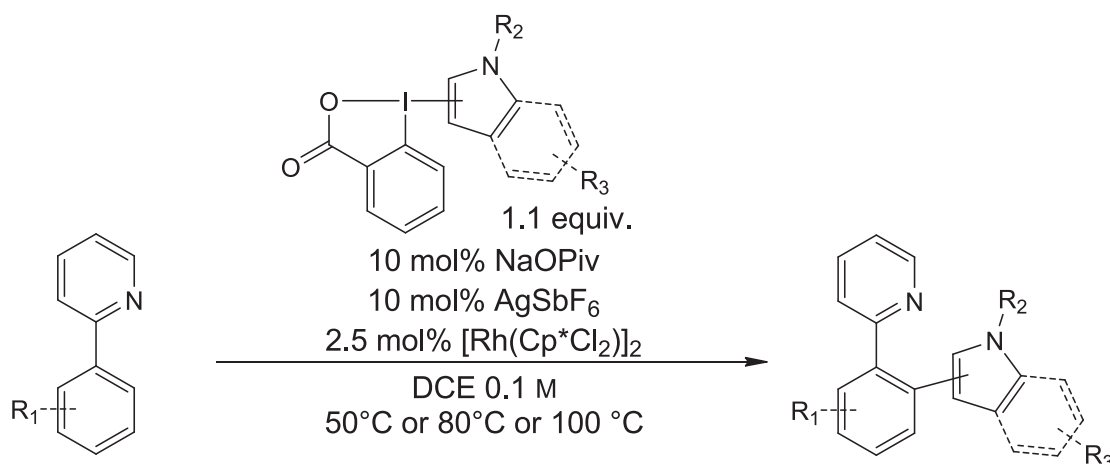
Entry	Substrate	Equiv.	Equiv. 8a	Catalyst (mol%)	Additive (mol%)	Solvent (M)/ T °C	Yield% ^a
1		1.5	1	-	2.0 equiv. TMSBr	HFIP (0.1 M)	-
2		1	1.5	Pd(OAc) ₂ (5)	-	MeCOOH (0.1 M)/110 °C	-



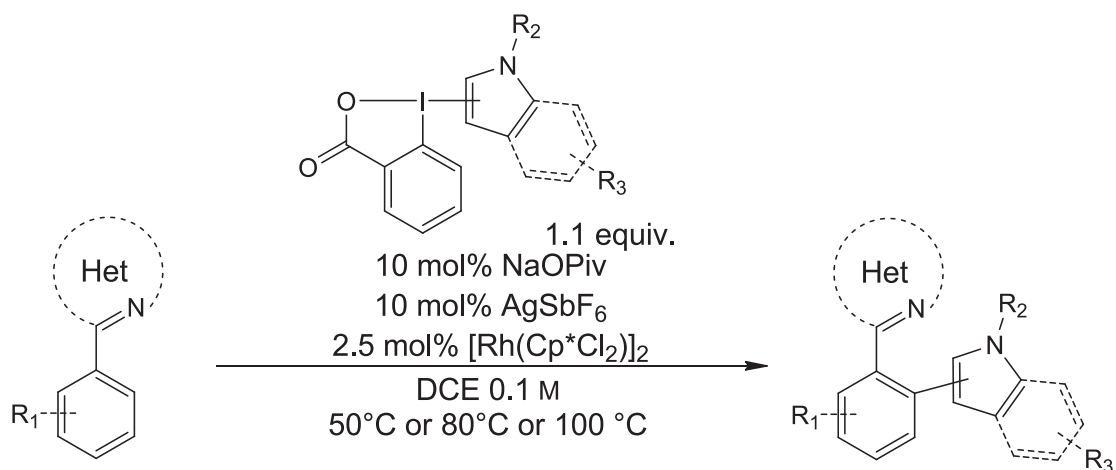
a) Reaction performed on 0.1 mmol of the limiting reagent; substrate (**X** mmol), Indole source **21** (**X** mmol), Catalyst (**X** mol%), Additive (**X** mol%) and Solvent (**X** M) at T °C.

3.4 Scope of the Rh-Catalyzed Indolization *via* C-H activation.

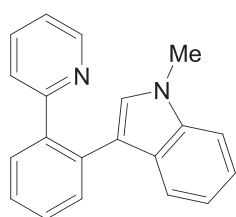
General Procedures GP3-GP4 for Rh-Catalyzed Hetero-arylation *via* C-H activation



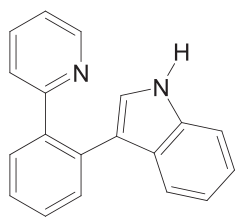
GP3: In a vial, the corresponding aryl-pyridine (0.300 mmol, 1.00 equiv.), the relative heterocyclic hypervalent iodine reagent (0.330 mmol, 1.10 equiv.), [Rh(Cp*Cl₂)]₂ (4.60 mg, 7.50 μmol, 2.5 mol%), AgSbF₆ (10.3 mg, 30.0 μmol, 10 mol%) and NaOPiv (3.70 mg, 30.0 μmol, 10 mol%) were dissolved in dry 1,2-DCE (3 ml, 0.1 M) under nitrogen. the reaction mixture was degassed (freeze-thaw-pump) and stirred at the reported T in °C overnight. The reaction mixture was then allowed to cool to r.t., the organic layer was washed with sat. aqueous NaHCO₃ (2ml), and the solvent was removed under reduced pressure. Flash column chromatography (Pentane:EtOAc) afforded the desired products **52-70**, **75**.



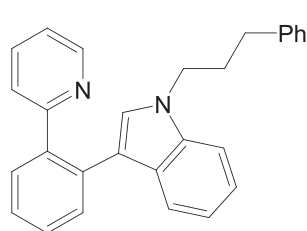
GP4: In a screw capped vial, the corresponding heterocycle (0.300 mmol, 1.00 equiv.), the relative heterocyclic hypervalent iodine reagent **21** (0.330 mmol, 1.10 equiv.), [Rh(Cp*Cl₂)]₂ (4.60 mg, 7.50 μmol, 2.5 mol%), AgSbF₆ (10.3 mg, 30.0 μmol, 10 mol%) and NaOPiv (3.70 mg, 30.0 μmol, 10 mol%) were dissolved in dry 1,2-DCE (3 ml, 0.1M) under nitrogen. the reaction mixture was degassed (freeze-thaw-pump) and stirred at the reported T in °C overnight. The reaction mixture was then allowed to cool to r.t., the organic layer was washed with sat. aqueous NaHCO₃ (2 mL), and the solvent was removed under reduced pressure. Flash column chromatography (Pentane:EtOAc) afforded the desired products **71-74**, **76-77**.



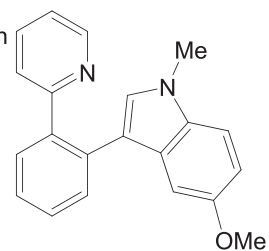
52
82% yield



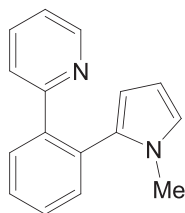
54
74% yield^d



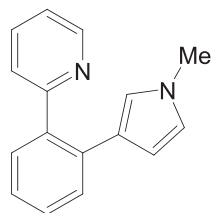
55
74% yield^b



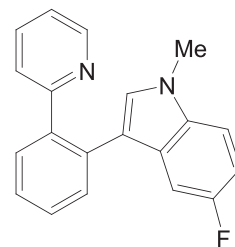
56
89% yield



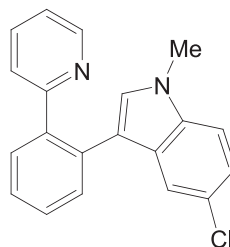
61
83% yield^b



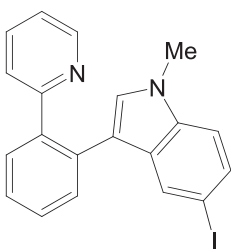
62
85% yield^b



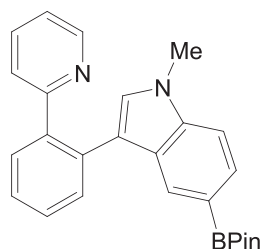
57
73% yield



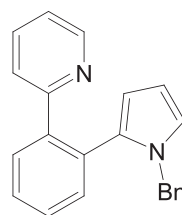
58
81% yield



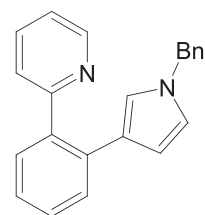
59
74 % yield



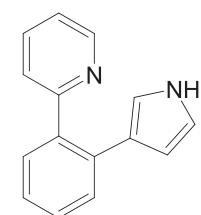
60
59% yield



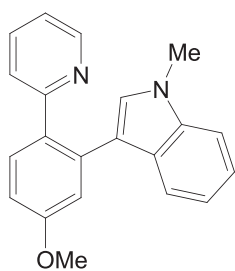
63
68% yield^b



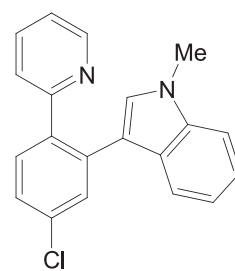
64
58% yield^b



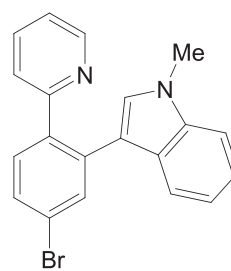
65
79% yield^b



66
88% yield



67
85% yield



68
84% yield

Figure S8: Scope with Aryl-pyridines.

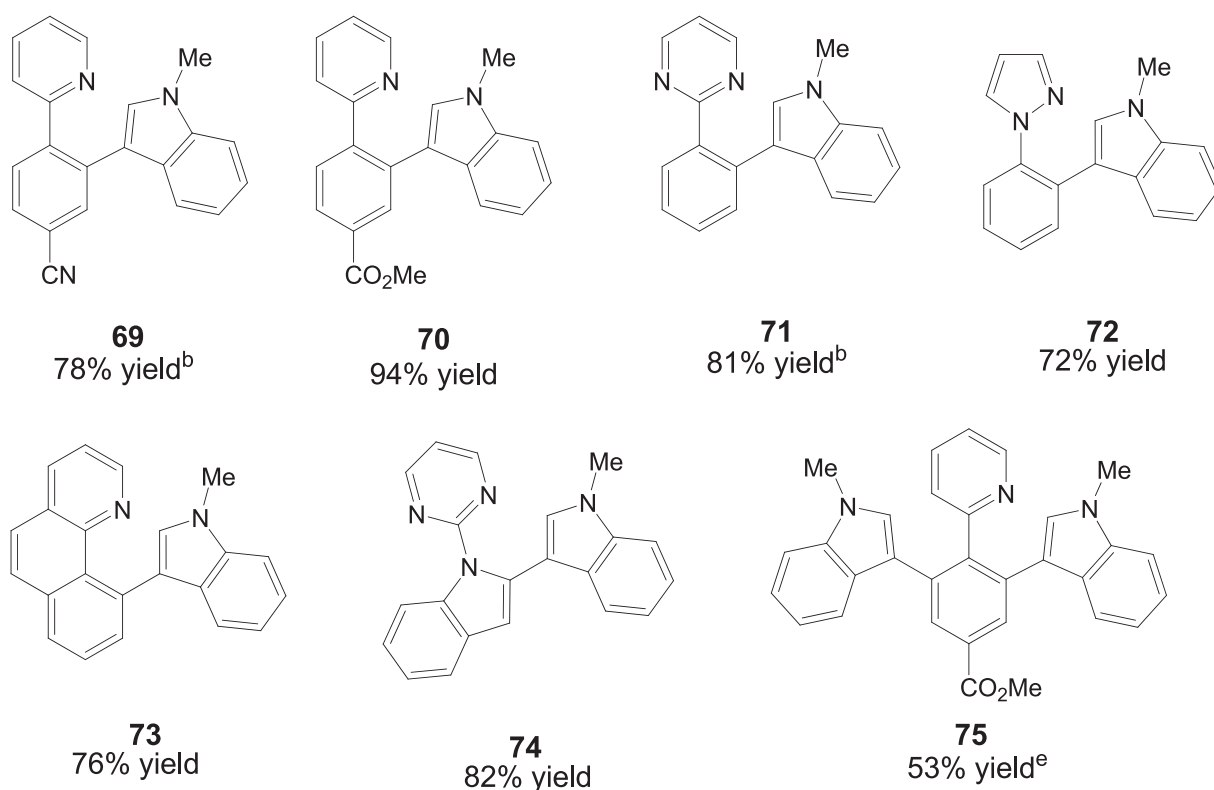
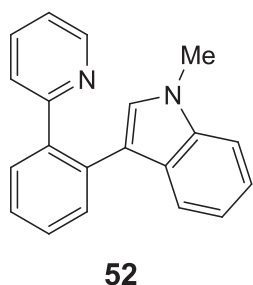


Figure S9: Scope with Aryl-pyridines (*I*).

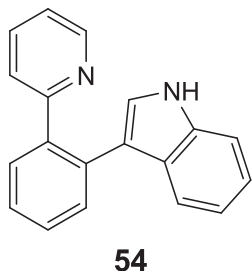
1-Methyl-3-(2-(pyridin-2-yl)phenyl)-1H-indole (**52**)



Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol, 1.00 equiv.) and with 1-(3-1-methyl-1H-indole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 2-(2-(1-methyl-1H-pyrrol-2-yl)phenyl)pyridine **52** (60.0 mg, 0.256 mmol, 85% yield) was obtained as a pale yellow oil. **R_f**: 0.48 (Pentane:EtOAc 4:1).

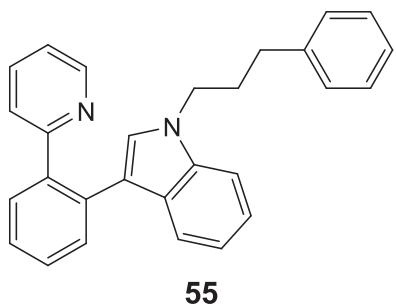
IR ν 3057 (w), 2934 (w), 1725 (w), 1586 (s), 1545 (m), 1461 (s), 1425 (s), 1377 (s), 1330 (m), 1219 (m), 1162 (w), 1091 (w), 1024 (w), 942 (w), 910 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.65 (m, 1H, Ar*H*), 7.73 (dd, *J* = 7.4, 1.7 Hz, 1H, Ar*H*), 7.59 (m, 1H, Ar*H*), 7.52 – 7.38 (m, 3H, Ar*H*), 7.35 – 7.22 (m, 2H, Ar*H*), 7.19 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H, Ar*H*), 7.11 – 6.94 (m, 3H, Ar*H*), 6.71 (s, 1H, NCHC), 3.70 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 159.9, 149.3, 139.8, 136.8, 135.1, 133.3, 131.0, 130.5, 128.4, 128.2, 127.0, 126.7, 124.9, 121.6, 121.2, 119.9, 119.5, 115.4, 109.1, 32.7. **HR-ESI-MS** 285.1388 ([*M*+*H*]⁺, C₂₀H₁₇N₂⁺; calc. for 285.1386).

3-(2-(pyridin-2-yl)phenyl)-1*H*-indole (**54**)



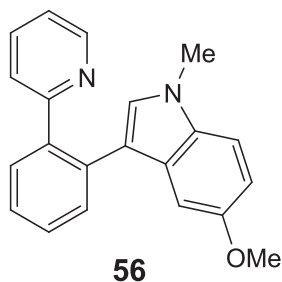
Starting from commercially available 2-phenylpyridine **8** (43.0 μ l, 0.300 mmol, 1.00 equiv.) and with 1-(3-1*H*-indole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **25** (120 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 2-(2-(1-methyl-1*H*-pyrrol-2-yl)phenyl)pyridine **54** (60.3 mg, 0.223 mmol, 74% yield) was obtained as a slightly brown foam. **Rf**: 0.30 (Pentane:EtOAc 4:1). **IR** ν 3409 (w), 3170 (w), 3058 (w), 2921 (w), 1668 (w), 1600 (m), 1589 (s), 1544 (w), 1489 (w), 1464 (s), 1332 (w), 1245 (m), 1153 (w), 1098 (w), 910 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.63 (m, 1H, Ar*H*), 8.40 (s, 1H, NH), 7.72 (dd, *J* = 7.3, 1.8 Hz, 1H, Ar*H*), 7.60 (dd, *J* = 7.3, 1.8 Hz, 1H, Ar*H*), 7.51 – 7.39 (m, 3H, Ar*H*), 7.33 – 7.22 (m, 2H, Ar*H*), 7.14 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H, Ar*H*), 7.02 (m, 3H, Ar*H*), 6.76 (d, *J* = 2.5 Hz, 1H, NHCHC). **¹³C NMR** (101 MHz, CDCl₃) δ 159.8, 149.0, 139.8, 135.9, 135.3, 133.3, 131.0, 130.5, 128.5, 126.9, 126.6, 125.0, 123.7, 122.0, 121.3, 119.9, 119.7, 116.7, 111.0. **HR-ESI-MS** 271.1233 ([M+H]⁺, C₁₉H₁₅N₂⁺; calc. for 271.1230).

1-(3-Phenylpropyl)-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole (**55**)



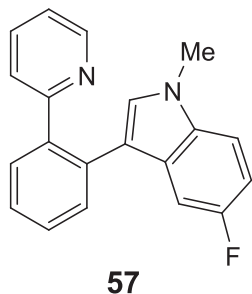
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol) and with 1-(3-1-(3-phenylpropyl)-1*H*-indole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **32** (159 mg, 0.330 mmol, 1.10 equiv.) at 80 °C, 1-(3-phenylpropyl)-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole **55** (86.0 mg, 0.221 mmol, 74% yield) was obtained as an orange oil. **Rf**: 0.48 (Pentane:EtOAc 4:1). **IR** ν 3059 (w), 3027 (w), 2932 (w), 1602 (w), 1585 (m), 1547 (w), 1496 (w), 1462 (s), 1424 (w), 1392 (w), 1372 (w), 1334 (w), 1167 (w), 1024 (w), 911 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.67 (m, 1H, Ar*H*), 7.76 (dd, *J* = 7.4, 1.7 Hz, 1H, Ar*H*), 7.67 (dd, *J* = 7.4, 1.5 Hz, 1H, Ar*H*), 7.58 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.51 (td, *J* = 7.4, 1.7 Hz, 1H, Ar*H*), 7.47 (td, *J* = 7.4, 1.5 Hz, 1H, Ar*H*), 7.34 – 7.19 (m, 6H, Ar*H*), 7.09 (m, 3H, Ar*H*), 7.06 – 7.01 (m, 2H, Ar*H*), 6.71 (s, 1H, CH₂NCHC), 4.04 (t, *J* = 6.8 Hz, 2H, PhCH₂CH₂CH₂N), 2.48 (dd, *J* = 8.6, 6.7 Hz, 2H, PhCH₂CH₂CH₂N), 2.08 (dq, *J* = 9.0, 6.9 Hz, 2H, PhCH₂CH₂CH₂N). **¹³C NMR** (101 MHz, CDCl₃) δ 160.0, 149.1, 140.8, 139.8, 136.0, 135.2, 133.3, 130.9, 130.5, 128.5, 128.3, 127.4, 127.3, 126.7, 126.1, 125.1, 121.6, 121.3, 119.9, 119.6, 115.2, 109.3, 45.4, 32.7, 31.3 (one Carbon signal not resolved). **HR-ESI-MS** 389.2016 ([M+H]⁺, C₂₈H₂₅N₂⁺; calc. for 389.2012).

5-Methoxy-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole (**56**)



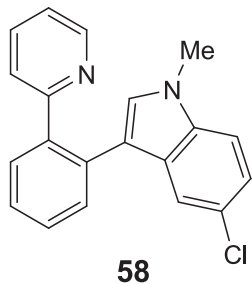
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol) and with 1-(3-5-methoxy-1-methyl-1*H*-indole)-1*H*-1 λ_3 -benzo[*b*]iodo-3(2*H*)-one **27** (134 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 5-methoxy-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole **56** (84.0 mg, 0.267 mmol, 89% yield) was obtained as a yellow oil. **Rf**: 0.40 (Pentane:EtOAc 4:1). **IR** ν 3051 (w), 2946 (w), 1585 (m), 1489 (s), 1463 (m), 1424 (m), 1295 (w), 1266 (s), 1228 (m), 1210 (s), 1181 (w), 1136 (m), 1088 (w), 1031 (m), 866 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.67 (dd, *J* = 4.9, 0.9 Hz, 1H, Ar*H*), 7.76 (dd, *J* = 7.2, 1.9 Hz, 1H, Ar*H*), 7.56 (dd, *J* = 7.2, 1.9 Hz, 1H, Ar*H*), 7.57 – 7.42 (m, 2H, Ar*H*), 7.26 (td, *J* = 7.7, 1.9 Hz, 1H, Ar*H*), 7.14 (d, *J* = 8.9 Hz, 1H, Ar*H*), 7.10 – 7.02 (m, 2H, Ar*H*), 6.84 (s, 1H, NCHC), 6.79 (dd, *J* = 8.9, 2.4 Hz, 1H, Ar*H*), 6.67 (d, *J* = 2.4 Hz, 1H, CCHCOMe), 3.71 (s, 3H, NCH₃), 3.64 (s, 3H, OCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 159.9, 153.9, 149.3, 139.4, 135.2, 133.4, 132.0, 131.0, 130.5, 128.5, 128.3, 126.9, 126.8, 124.9, 121.3, 115.3, 112.2, 109.8, 100.8, 55.6, 32.9. **HR-ESI-MS** 315.1493 ([M+H]⁺, C₂₁H₁₉N₂O⁺; calc. for 315.1492).

5-Fluoro-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole (**57**)



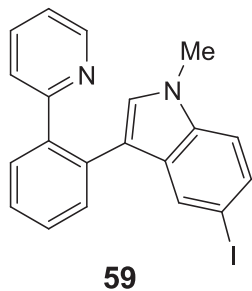
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol) and with 1-(3-5-fluoro-1-methyl-1*H*-indole)-1*H*-1 λ_3 -benzo[*b*]iodo-3(2*H*)-one **28** (130 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 5-fluoro-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole **57** (66.0 mg, 0.218 mmol, 73% yield) was obtained as a yellow oil. **Rf**: 0.40 (Pentane:EtOAc 4:1). **IR** ν 3063 (w), 2930 (w), 1624 (m), 1585 (m), 1488 (s), 1464 (m), 1425 (m), 1292 (w), 1192 (s), 1123 (m), 1060 (w), 873 (s). **¹H NMR** (400 MHz, CDCl₃) δ 8.65 (d, *J* = 4.9 Hz, 1H, Ar*H*), 7.71 (d, *J* = 7.2 Hz, 1H, Ar*H*), 7.55 (d, *J* = 7.2 Hz, 1H, Ar*H*), 7.51 – 7.38 (m, 2H), 7.33 (t, *J* = 7.7 Hz, 1H, Ar*H*), 7.17 (dd, *J* = 9.0, 4.3 Hz, 1H, Ar*H*), 7.08 (t, *J* = 6.3 Hz, 1H, Ar*H*), 7.08 – 6.97 (m, 2H, Ar*H*), 6.91 (t, *J* = 9.0 Hz, 1H, Ar*H*), 6.77 (s, 1H, NCHC), 3.70 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 159.8, 158.0 (d, *J* = 234.6 Hz), 149.3, 139.7, 135.2, 133.4, 132.9, 130.8, 130.6, 129.7, 128.5, 127.3 (d, *J* = 9.9 Hz), 126.9, 124.8, 121.3, 115.5 (d, *J* = 4.9 Hz), 110.0 (d, *J* = 26.5 Hz), 109.7 (d, *J* = 9.7 Hz), 104.7 (d, *J* = 24.2 Hz), 33.0. **¹⁹F NMR** (376 MHz, CDCl₃) δ -125.1. **HR-ESI-MS** 303.1295 ([M+H]⁺, C₂₀H₁₆FN₂⁺; calc. for 303.1292).

5-Chloro-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole (**58**)



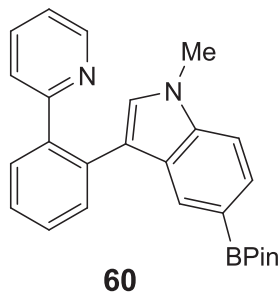
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol) and with 1-(3-5-chloro-1-methyl-1*H*-indole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **29** (136 mg, 0.330 mmol, 1.10 equiv.) at 50°C, 5-fluoro-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole **58** (77.0 mg, 0.242 mmol, 81% yield) was obtained as a yellow oil. **Rf**: 0.36 (Pentane:EtOAc 4:1). **IR** ν 3055 (w), 3014 (w), 2924 (w), 1586 (w), 1543 (w), 1477 (s), 1424 (m), 1374 (w), 1288 (w), 1218 (w), 1152 (w), 1096 (w), 1058 (w), 953 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.65 (m, 1H, Ar*H*), 7.72 (dd, *J* = 7.3, 1.8 Hz, 1H, Ar*H*), 7.55 (m, 1H, Ar*H*), 7.46 (pd, *J* = 7.3, 1.8 Hz, 2H, Ar*H*), 7.38 – 7.31 (m, 2H, Ar*H*), 7.17 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.14 – 7.07 (m, 2H, Ar*H*), 7.04 (m, 1H, Ar*H*), 6.75 (s, 1H, NCHC), 3.69 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 159.6, 149.0, 139.5, 135.6, 135.2, 132.7, 131.0, 130.6, 129.4, 128.7, 128.0, 127.1, 125.5, 124.9, 121.9, 121.4, 119.3, 115.2, 110.2, 33.0. **HR-ESI-MS** 319.1006 ([M+H]⁺, C₂₀H₁₆ClN₂⁺; calc. for 319.0997).

5-Iodo-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole (**59**)



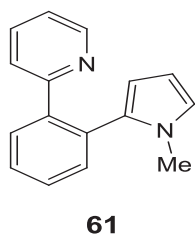
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol) and with 1-(3-5-iodo-1-methyl-1*H*-indole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **30** (166 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 5-Iodo-1-methyl-3-(2-(pyridin-2-yl)phenyl)-1*H*-indole **59** (91.0 mg, 0.222 mmol, 74% yield) was obtained as a yellow oil. **Rf**: 0.45 (Pentane:EtOAc 4:1). **IR** ν 3058 (w), 2920 (w), 1606 (w), 1585 (m), 1474 (s), 1422 (m), 1371 (w), 1287 (w), 1266 (w), 1217 (w), 1148 (w), 1092 (w), 1024 (w), 943 (w), 874 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.66 (dd, *J* = 5.0, 0.9 Hz, 1H, Ar*H*), 7.71 (m, 1H, Ar*H*), 7.65 (d, *J* = 1.6 Hz, 1H, Ar*H*), 7.53 (m, 1H, Ar*H*), 7.50 – 7.42 (m, 2H, Ar*H*), 7.39 (dd, *J* = 8.5, 1.6 Hz, 1H, Ar*H*), 7.32 (td, *J* = 7.7, 1.9 Hz, 1H, Ar*H*), 7.08 (ddd, *J* = 7.7, 5.0, 1.1 Hz, 1H, Ar*H*), 7.07 – 6.97 (m, 2H, Ar*H*), 6.70 (s, 1H, NCHC), 3.67 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 159.7, 149.3, 139.8, 135.7, 135.2, 132.5, 130.9, 130.5, 129.8, 129.2, 128.7, 128.7, 128.5, 127.0, 124.7, 121.4, 114.9, 111.1, 83.2, 32.9. **HR-ESI-MS** 411.0348 ([M+H]⁺, C₂₀H₁₆IN₂⁺; calc. for 411.0353).

1-Methyl-3-(2-(pyridin-2-yl)phenyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole (60)



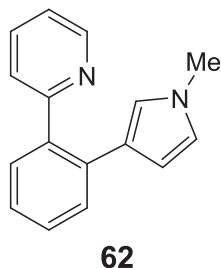
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol) and with 1-(3-1-methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole)-1H-1 λ_3 -benzo[*b*]iodo-3(2H)-one **31** (166 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 1-Methyl-3-(2-(pyridin-2-yl)phenyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole **60** (73.0 mg, 0.178 mmol, 59% yield) was obtained as a yellow oil. **Rf**: 0.30 (Pentane:EtOAc 4:1). **IR** ν 3063 (w), 2978 (w), 2940 (w), 2245 (w), 2214 (w), 1608 (m), 1605 (m), 1568 (w), 1463 (m), 1438 (m), 1383 (s), 1349 (s), 1311 (s), 1273 (m), 1142 (s), 1097 (m), 967 (m), 910 (s), 866 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.64 (d, *J* = 5.0 Hz, 1H, ArH), 8.00 (s, 1H, ArH), 7.71 (d, *J* = 7.5 Hz, 1H, ArH), 7.64 (dd, *J* = 8.3, 1.1 Hz, 1H, ArH), 7.61 (m, 1H, ArH), 7.46 (td, *J* = 7.4, 1.7 Hz, 1H, ArH), 7.41 (td, *J* = 7.4, 1.6 Hz, 1H, ArH), 7.29 – 7.26 (m, 2H, ArH), 7.00 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H, ArH), 6.95 (dt, *J* = 7.9, 1.0 Hz, 1H, ArH), 6.62 (s, 1H, ArH), 3.68 (s, 3H, NCH₃), 1.34 (s, 12H, BPin). **¹³C NMR** (101 MHz, CDCl₃) δ 159.9, 149.1, 140.0, 138.6, 135.0, 133.1, 131.2, 130.3, 128.4, 128.2, 127.7, 127.7, 126.9, 126.7, 124.9, 121.1, 116.0, 108.5, 83.3, 32.6, 24.8 (one aromatic Carbon signal not resolved). **HR-ESI-MS** 411.2248 ([M+H]⁺, C₂₆H₂₈BN₂O₂⁺; calc. for 411.2238).

2-(2-(1-methyl-1H-pyrrol-2-yl)phenyl)pyridine (61)



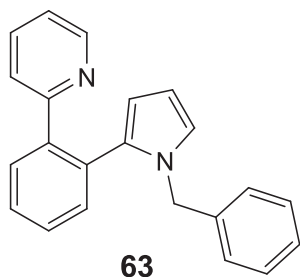
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol, 1.00 equiv.) and with 1-(2-1-methyl-1H-pyrrole)-1H-1 λ_3 -benzo[*b*]iodo-3(2H)-one **35a** (108 mg, 0.330 mmol, 1.10 equiv.) at 80 °C, 2-(2-(1-methyl-1H-pyrrol-2-yl)phenyl)pyridine **61** (60.0 mg, 0.256 mmol, 85% yield) was obtained as a pale yellow oil. **Rf**: 0.42 (Pentane:EtOAc 4:1). **IR** ν 3098 (w), 3059 (w), 2926 (m), 2854 (w), 1707 (w), 1585 (s), 1473 (s), 1429 (s), 1310 (s), 1239 (w), 1090 (m), 1056 (m), 1024 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.67 (m, 1H, ArH), 7.86 (d, *J* = 7.5 Hz, 1H, ArH), 7.55 – 7.40 (m, 4H, ArH), 7.14 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H, ArH), 6.80 (m, 1H, ArH), 6.51 (t, *J* = 2.3 Hz, 1H, ArH), 6.18 – 6.15 (m, 2H, ArH), 2.90 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 158.6, 149.5, 140.0, 135.7, 133.2, 131.8, 131.5, 130.1, 128.5, 128.4, 123.7, 122.2, 121.5, 109.2, 107.7, 33.8. **HR-ESI-MS** 235.1233 ([M+H]⁺, C₁₆H₁₅N₂⁺; calc. for 235.1230).

2-(2-(1-Methyl-1H-pyrrol-3-yl)phenyl)pyridine (**62**)



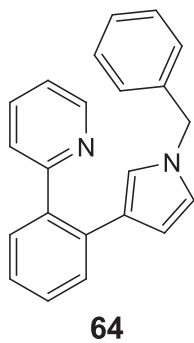
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol, 1.00 equiv.) and with 1-(3-(1-methyl-1H-pyrrole)-1H-1 λ_3 -benzo[*b*]iodo-3(2H)-one **35b** (108 mg, 0.330 mmol, 1.10 equiv.) at 80°C, 2-(2-(1-Methyl-1H-pyrrol-3-yl)phenyl)pyridine **62** (60.0 mg, 0.256 mmol, 85% yield) was obtained as a yellow oil. **Rf**: 0.38 (Pentane:EtOAc 4:1). **IR** ν 3056 (w), 3007 (w), 2943 (w), 1586 (s), 1551 (m), 1508 (m), 1463 (s), 1424 (s), 1361 (m), 1260 (w), 1202 (s), 1150 (w), 1087 (w), 1024 (w), 990 (w), 926 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.67 (d, J = 5.0 Hz, 1H, ArH), 7.57 – 7.46 (m, 3H, ArH), 7.37 (t, J = 7.5 Hz, 1H, ArH), 7.31 (d, J = 7.5 Hz, 1H, ArH), 7.22 (d, J = 7.9 Hz, 1H, ArH), 7.18 (dd, J = 7.4, 5.1 Hz, 1H, ArH), 6.43 (t, J = 2.5 Hz, 1H, ArH), 6.30 (d, J = 1.6 Hz, 1H, ArH), 5.80 (d, J = 1.6 Hz, 1H, ArH), 3.54 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 160.6, 149.1, 138.7, 135.2, 134.8, 130.2, 129.3, 128.3, 125.8, 125.2, 123.8, 121.5, 121.3, 120.6, 109.2, 36.1. **HR-ESI-MS** 235.1230 ([M+H]⁺, C₁₆H₁₅N₂⁺; calc. for 235.1230).

2-(2-(1-benzyl-1H-pyrrol-2-yl)phenyl)pyridine (**63**)



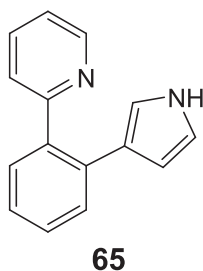
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol, 1.00 equiv.) and with 1-(2-(1-benzyl-1H-pyrrole)-1H-1 λ_3 -benzo[*b*]iodo-3(2H)-one **36a** (133 mg, 0.330 mmol, 1.10 equiv.) at 80 °C, 2-(2-(1-benzyl-1H-pyrrol-2-yl)phenyl)pyridine **63** (63.0 mg, 0.203 mmol, 68% yield) as a pale yellow oil. **Rf**: 0.32 (Pentane:EtOAc 4:1). **IR** ν 3062 (m), 3029 (w), 2925 (w), 1585 (s), 1471 (s), 1427 (s), 1311 (m), 1298 (m), 1236 (m), 1153 (w), 1076 (m), 1024 (m), 989 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.68 (d, J = 4.9 Hz, 1H, ArH), 7.85 (m, 1H, ArH), 7.53 – 7.42 (m, 2H, ArH), 7.42 – 7.33 (m, 2H, ArH), 7.17 – 7.13 (m, 4H, ArH), 6.83 (d, J = 7.9 Hz, 1H, ArH), 6.72 (dd, J = 6.6, 2.9 Hz, 2H, ArH), 6.52 (m, 1H, ArH), 6.24 – 6.13 (m, 2H, ArH), 4.45 (s, 2H, NCH₂Ph). **¹³C NMR** (101 MHz, CDCl₃) δ 158.7, 149.5, 140.2, 138.1, 135.8, 133.2, 132.1, 131.7, 130.3, 128.6, 128.6, 128.4, 127.3, 127.2, 124.2, 121.7, 110.1, 108.3, 50.6. (2 Cs overlapping at 121.7, shown by HSQC). **HR-ESI-MS** 311.1542 ([M+H]⁺, C₂₂H₁₉N₂⁺; calc. for 311.1543).

2-(2-(1-Benzyl-1*H*-pyrrol-3-yl)phenyl)pyridine (**64**)



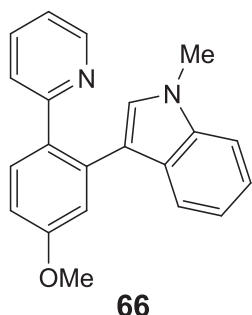
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol, 1.00 equiv.) and with 1-(3-(1-benzyl-1*H*-pyrrole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **36b** (133 mg, 0.330 mmol, 1.10 equiv.) at 80 °C, 2-(2-(1-Benzyl-1*H*-pyrrol-3-yl)phenyl)pyridine **64** (54.0 mg, 0.174 mmol, 58% yield) was obtained as a pale yellow oil. **Rf**: 0.30 (Pentane:EtOAc 4:1). **IR** ν 3062 (m), 2925 (m), 2854 (w), 1708 (m), 1586 (s), 1562 (m), 1498 (s), 1463 (s), 1425 (s), 1355 (m), 1190 (m), 1082 (m), 1025 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.62 (m, 1H, Ar*H*), 7.51 – 7.45 (m, 3H, Ar*H*), 7.38 (td, *J* = 7.5, 1.6 Hz, 1H, Ar*H*), 7.34 – 7.26 (m, 4H, Ar*H*), 7.20 (d, *J* = 7.9 Hz, 1H, Ar*H*) 7.13 (ddd, *J* = 7.4, 4.9, 1.2 Hz, 1H, Ar*H*), 7.03 – 6.97 (m, 2H, Ar*H*), 6.54 (t, *J* = 2.5 Hz, 1H, Ar*H*), 6.25 (t, *J* = 1.8 Hz, 1H, Ar*H*), 5.99 (dd, *J* = 2.5, 1.8 Hz, 1H, Ar*H*), 4.92 (s, 2H, NCH₂Ph). **¹³C NMR** (101 MHz, CDCl₃) δ 160.5, 149.1, 138.8, 137.9, 135.2, 134.8, 130.1, 129.4, 128.6, 128.3, 127.6, 126.9, 126.0, 125.2, 123.9, 121.3, 121.0, 120.4, 109.4, 53.3. **HR-ESI-MS** 311.1545 ([M+H]⁺, C₂₂H₁₉N₂⁺; calc. for 311.1543).

2-(2-(1*H*-Pyrrol-3-yl)phenyl)pyridine (**65**)



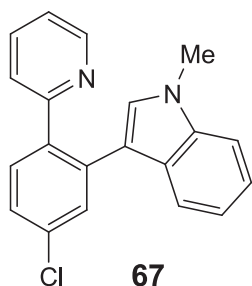
Starting from commercially available 2-phenylpyridine **49** (43.0 μ l, 0.300 mmol, 1.00 equiv.) and with 1-(3-1*H*-pyrrole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **37** (103 mg, 0.330 mmol, 1.10 equiv.) in a mixture of 1,2-DCE:MeOH (2:1, 0.1M) at 50 °C, 2-(2-(1*H*-pyrrol-3-yl)phenyl)pyridine **65** (52.0 mg, 0.236 mmol, 79% yield) was obtained as a light brown foam. **Rf**: 0.42 (Pentane:EtOAc 4:1). **IR** ν 3191 (m), 3054 (m), 2928 (w), 1601 (s), 1589 (s), 1562 (m), 1505 (m), 1464 (s), 1426 (s), 1267 (w), 1152 (w), 1078 (w), 1028 (m), 996 (w), 917 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.67 (m, 1H, Ar*H*), 8.29 (m, 1H, NH), 7.57 – 7.47 (m, 3H, Ar*H*), 7.40 (dd, *J* = 8.2, 6.8 Hz, 1H, Ar*H*), 7.32 (t, *J* = 7.3 Hz, 1H, Ar*H*), 7.23 – 7.15 (m, 2H, Ar*H*), 6.62 (d, *J* = 2.6 Hz, 1H, Ar*H*), 6.43 (d, *J* = 2.6 Hz, 1H, Ar*H*), 5.95 (dd, *J* = 2.9, 1.6 Hz, 1H, Ar*H*). **¹³C NMR** (101 MHz, CDCl₃) δ 160.6, 149.2, 139.0, 135.2, 134.7, 130.2, 129.6, 128.4, 126.1, 125.2, 123.8, 121.4, 117.6, 116.8, 109.3. **HR-ESI-MS** 221.1077 ([M+H]⁺, C₁₅H₁₃N₂⁺; calc. for 221.1073).

3-(5-Methoxy-2-(pyridin-2-yl)phenyl)-1-methyl-1*H*-indole (**66**)



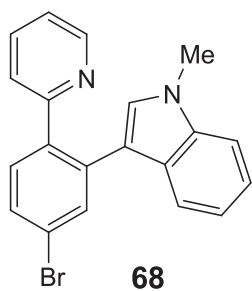
Starting from commercially available 2-(4-methoxyphenyl)pyridine (55.6 mg, 0.300 mmol) and with 1-(3-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 3-(5-methoxy-2-(pyridin-2-yl)phenyl)-1-methyl-1*H*-indole **66** (83.0 mg, 0.264 mmol, 88% yield) was obtained as a yellow oil. **Rf**: 0.38 (Pentane:EtOAc 4:1). **IR** ν 3049 (w), 2933 (w), 2834 (w), 1602 (s), 1568 (m), 1463 (s), 1426 (m), 1278 (s), 1232 (s), 1210 (m), 1062 (m), 1017 (m), 844 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.64 (d, *J* = 5.0 Hz, 1H, Ar*H*), 7.70 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.45 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.31 – 7.23 (m, 2H, Ar*H*), 7.20 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.13 (d, *J* = 2.7 Hz, 1H, Ar*H*), 7.06 – 6.95 (m, 4H, Ar*H*), 6.73 (s, 1H, CH₃NCHC), 3.89 (s, 3H, NCH₃), 3.71 (s, 3H, OCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 159.6, 159.4, 148.9, 136.7, 135.2, 134.6, 132.3, 131.9, 128.2, 126.8, 125.0, 121.6, 120.8, 119.9, 119.5, 115.9, 115.3, 112.6, 109.1, 55.3, 32.8. **HR-ESI-MS** 315.1494 ([M+H]⁺, C₂₁H₁₉N₂O⁺; calc. for 315.1492).

3-(5-Chloro-2-(pyridin-2-yl)phenyl)-1-methyl-1*H*-indole (**67**)



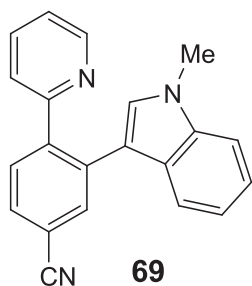
Starting from commercially available 2-(4-chlorophenyl)pyridine (57.0 mg, 0.300 mmol) and with 1-(3-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 3-(5-chloro-2-(pyridin-2-yl)phenyl)-1-methyl-1*H*-indole **67** (81.2 mg, 0.255 mmol, 85% yield) was obtained as a yellow oil. **Rf**: 0.40 (Pentane:EtOAc 4:1). **IR** ν 3055 (w), 2926 (w), 1595 (s), 1566 (m), 1476 (m), 1461 (s), 1427 (w), 1329 (m), 1219 (w), 1163 (w), 1100 (m), 1026 (w), 913 (w), 830 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.65 (m, 1H, Ar*H*), 7.68 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.59 (d, *J* = 2.2 Hz, 1H, Ar*H*), 7.40 (dd, *J* = 8.3, 2.2 Hz, 1H, Ar*H*), 7.37 (dd, *J* = 8.0, 1.0 Hz, 1H, Ar*H*), 7.30 (dd, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.27 (m, 1H, Ar*H*), 7.19 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H, Ar*H*), 7.08 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H, Ar*H*), 7.04 – 6.99 (m, 2H, Ar*H*), 6.75 (s, 1H, NCHC), 3.71 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 158.7, 149.2, 137.9, 136.8, 135.4, 135.1, 134.3, 132.0, 130.7, 128.4, 126.7, 126.6, 124.9, 121.8, 121.5, 119.8, 119.7, 114.3, 109.2, 32.8. **HR-ESI-MS** 319.0999 ([M+H]⁺, C₂₀H₁₆ClN₂⁺; calc. for 319.0997).

3-(5-Bromo-2-(pyridin-2-yl)phenyl)-1-methyl-1*H*-indole (**68**)



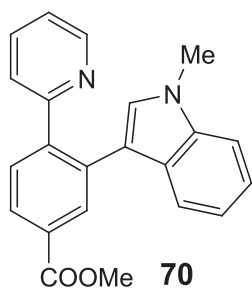
Starting from commercially available 2-(4-bromophenyl)pyridine (70.2 mg, 0.300 mmol) and with 1-(3-1-methyl-1H-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 3-(5-methoxy-2-(pyridin-2-yl)phenyl)-1-methyl-1*H*-indole **68** (91.0 mg, 0.251 mmol, 84% yield) was obtained as a yellow oil. **Rf**: 0.40 (Pentane:EtOAc 4:1). **IR** ν 2956 (w), 2929 (w), 2851 (w), 1678 (w), 1592 (m), 1510 (m), 1453 (m), 1453 (m), 1434 (s), 1399 (s), 1364 (s), 1264 (m), 1108 (m), 1031 (m), 956 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.66 (m, 1H, Ar*H*), 7.75 (d, *J* = 2.0 Hz, 1H, Ar*H*), 7.63 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.56 (dd, *J* = 8.3, 2.0 Hz, 1H, Ar*H*), 7.36 – 7.31 (m, 2H, Ar*H*), 7.28 (dt, *J* = 8.2, 0.9 Hz, 1H, Ar*H*), 7.19 (ddd, *J* = 8.2, 6.9, 0.9 Hz, 1H, Ar*H*), 7.11 (t, *J* = 6.3 Hz, 1H, Ar*H*), 7.04 (d, *J* = 8.0 Hz, 1H, Ar*H*), 6.99 (m, 1H, Ar*H*), 6.77 (s, 1H, NCHC), 3.72 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 158.7, 149.3, 138.5, 136.7, 135.4, 135.2, 133.5, 132.1, 129.6, 128.3, 126.5, 124.7, 122.4, 121.8, 121.5, 119.7, 119.6, 114.2, 109.2, 32.7. **HR-ESI-MS** 363.0490 ([M+H]⁺, C₂₀H₁₆⁷⁹BrN₂⁺; calc. for 363.0491).

3-(1-Methyl-1*H*-indol-3-yl)-4-(pyridin-2-yl)benzonitrile (**69**)



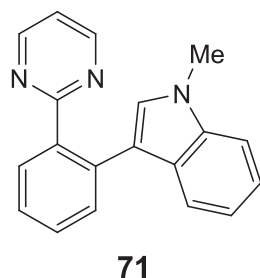
Starting from commercially available 4-(pyridin-2-yl)benzonitrile (54.0 mg, 0.300 mmol) and with 1-(3-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 80 °C, 3-(1-methyl-1*H*-indol-3-yl)-4-(pyridin-2-yl)benzonitrile **69** (72.0 mg, 0.233 mmol, 78% yield) was obtained as a yellow oil. **Rf**: 0.35 (Pentane:EtOAc 4:1). **IR** ν 3053 (w), 2932 (w), 2230 (m), 1587 (m), 1558 (w), 1475 (m), 1463 (m), 1330 (w), 1266 (s), 1224 (w), 1160 (w), 1091 (w), 1026 (w), 902 (w), 839 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.70 (m, 1H, Ar*H*), 7.88 (d, *J* = 1.7 Hz, 1H, Ar*H*), 7.83 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.69 (dd, *J* = 8.0, 1.7 Hz, 1H, Ar*H*), 7.36 – 7.27 (m, 3H, Ar*H*), 7.21 (ddd, *J* = 8.3, 7.0, 1.1 Hz, 1H, Ar*H*), 7.13 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H, Ar*H*), 7.05 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.02 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H, Ar*H*), 6.77 (s, 1H, NCHC), 3.73 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 157.9, 149.6, 143.6, 136.7, 135.6, 134.8, 134.5, 131.5, 129.8, 128.4, 126.3, 124.7, 122.2, 122.0, 120.1, 119.3, 118.9, 113.3, 112.1, 109.4, 32.9. **HR-ESI-MS** 310.1344 ([M+H]⁺, C₂₁H₁₆N₃⁺; calc. for 310.1339).

Methyl 3-(1-methyl-1*H*-indol-3-yl)-4-(pyridin-2-yl)benzoate (**70**)



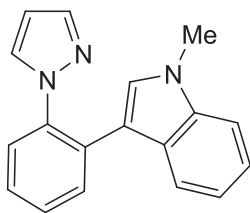
Starting from methyl 4-(pyridin-2-yl)benzoate **121** (64.0 mg, 0.300 mmol) and with 1-(3-1-methyl-1H-indole)-1H-1λ₃-benzo[*b*]iodo-3(2H)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 50°C, methyl 3-(1-methyl-1H-indol-3-yl)-4-(pyridin-2-yl)benzoate **70** (94.0 mg, 0.275 mmol, 92% yield) was obtained as an orange oil. Rf: 0.33 (Pentane:EtOAc 4:1). **¹H NMR** (400 MHz, CDCl₃) δ 8.61 (dd, *J* = 5.1, 1.6 Hz, 1H, Ar*H*), 8.20 (d, *J* = 1.7 Hz, 1H, Ar*H*), 7.99 (dd, *J* = 8.1, 1.8 Hz, 1H, Ar*H*), 7.72 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.26 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.24 – 7.16 (m, 2H, Ar*H*), 7.09 (t, *J* = 7.6 Hz, 1H, Ar*H*), 7.03 – 6.96 (m, 2H, Ar*H*), 6.90 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.71 (s, 1H, NCHC), 3.85 (s, 3H, COOMe), 3.61 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 167.0, 158.8, 149.4, 143.8, 136.8, 135.3, 133.7, 132.3, 130.7, 129.9, 128.3, 127.6, 126.7, 124.7, 121.8, 121.7, 119.7, 114.7, 109.1, 52.1, 32.8 (two aromatic Carbon signals overlapping at 119.7). **IR** ν 3052 (w), 2950 (w), 2252 (w), 2218 (w), 1718 (s), 1587 (m), 1436 (m), 1365 (m), 1330 (m), 1286 (s), 1251 (s), 1162 (m), 1113 (m), 994 (w), 911 (s). **HR-ESI-MS** 343.1438 ([M+H]⁺, C₂₂H₁₉N₂O₂⁺; calc. for 343.1441).

1-Methyl-3-(2-(pyrimidin-2-yl)phenyl)-1H-indole (71)



Starting from commercially available 2-phenylpyrimidine (47.0 mg, 0.300 mmol) and with 1-(3-1-methyl-1H-indole)-1H-1λ₃-benzo[*b*]iodo-3(2H)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 80 °C, 1-methyl-3-(2-(pyrimidin-2-yl)phenyl)-1H-indole **71** (69.0 mg, 0.242 mmol, 81% yield) was obtained as a yellow oil. Rf: 0.40 (Pentane:EtOAc 4:1). **IR** ν 3048 (w), 2932 (w), 1599 (w), 1568 (s), 1554 (m), 1473 (w), 1414 (s), 1377 (w), 1330 (w), 1268 (w), 1221 (w), 1162 (w), 1135 (w), 1015 (w), 943 (w), 822 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.58 (d, *J* = 4.9 Hz, 2H, Pyrimidine*H*), 7.84 (dd, *J* = 7.7, 1.5 Hz, 1H, Ar*H*), 7.59 (dd, *J* = 7.7, 1.5 Hz, 1H, Ar*H*), 7.51 (m, 1H, Ar*H*), 7.44 (td, *J* = 7.5, 1.5 Hz, 1H, Ar*H*), 7.24 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.10 (dd, *J* = 9.3, 7.5 Hz, 2H, Ar*H*), 7.03 (s, 1H, NCHCl), 7.00 (t, *J* = 4.9 Hz, 1H, Ar*H*), 6.84 (t, *J* = 7.5 Hz, 1H, Ar*H*), 3.76 (s, 3H, NCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 168.5, 156.7, 138.1, 136.7, 134.1, 131.3, 130.7, 129.4, 127.5, 126.8, 126.5, 121.3, 119.3, 119.2, 118.2, 116.2, 109.0, 32.8 (two aromatic Carbon signals overlapping at 156.7). **HR-ESI-MS** 286.1344 ([M+H]⁺, C₁₉H₁₆N₃⁺; calc. for 286.1339).

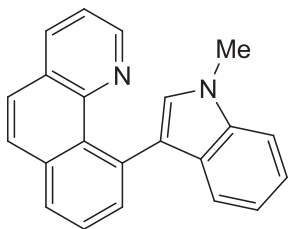
3-(2-(1H-Pyrazol-1-yl)phenyl)-1-methyl-1H-indole (72)



72

Starting from commercially available 1-phenyl-1H-pyrazole (43.0 mg, 0.300 mmol) and with 1-(3-1-methyl-1H-indole)-1H-1λ₃-benzo[*b*]iodo-3(2H)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 80 °C, 3-(2-(1H-pyrazol-1-yl)phenyl)-1-methyl-1H-indole **72** (59.0 mg, 0.216 mmol, 72% yield) was obtained as a yellow oil. **Rf**: 0.40 (Pentane:EtOAc 4:1). **IR** ν 3049 (w), 2926 (m), 2853 (w), 1680 (w), 1615 (w), 1604 (w), 1548 (m), 1518 (s), 1473 (s), 1423 (w), 1394 (s), 1378 (s), 1329 (s), 1264 (w), 1221 (m), 1089 (m), 1045 (s), 1019 (m), 936 (s). **¹H NMR** (400 MHz, CDCl₃) δ 7.69 (dd, *J* = 7.8, 1.6 Hz, 1H, *ArH*), 7.67 (d, *J* = 1.7 Hz, 1H, *ArH*), 7.62 (dd, *J* = 7.8, 1.6 Hz, 1H, *ArH*), 7.52 – 7.44 (m, 2H, *ArH*), 7.40 (td, *J* = 7.8, 1.6 Hz, 1H, *ArH*), 7.31 (d, *J* = 8.2 Hz, 1H, *ArH*), 7.25 – 7.20 (m, 2H, *ArH*), 7.07 (m, 1H, *ArH*), 6.60 (s, 1H, *NCHC*), 6.15 (m, 1H, *ArH*), 3.72 (s, 3H, *NCH*₃). **¹³C NMR** (101 MHz, CDCl₃) δ 139.9, 138.5, 136.7, 131.1, 131.0, 130.6, 128.2, 127.6, 127.0, 126.9, 126.6, 121.8, 119.9, 119.3, 112.0, 109.3, 106.2, 32.8. **HR-ESI-MS** 274.1343 ([*M*+*H*]⁺, C₁₈H₁₆N₃⁺; calc. for 274.1339).

10-(1-Methyl-1H-indol-3-yl)benzo[*h*]quinoline (73)

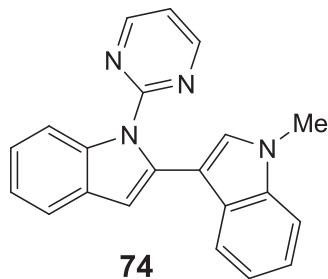


73

Starting from commercially available benzo[*h*]quinoline (54.0 mg, 0.300 mmol) and with 1-(3-1-methyl-1H-indole)-1H-1λ₃-benzo[*b*]iodo-3(2H)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 10-(1-methyl-1H-indol-3-yl)benzo[*h*]quinoline **73** (70.0 mg, 0.227 mmol, 76% yield) was obtained as a light yellow oil. **Rf**: 0.40 (Pentane:EtOAc 4:1). **IR** ν 3046 (m), 2929 (m), 1677 (w), 1615 (w), 1588 (m), 1569 (m), 1475 (s), 1418 (s), 1375 (s), 1323 (s), 1263 (w), 1230 (s), 1161 (w), 1129 (w), 1014 (w), 910 (m). **¹H NMR** (400 MHz, CDCl₃) δ 8.27 (d, *J* = 2.4 Hz, 1H, *ArH*), 8.10 (dd, *J* = 8.0, 1.9 Hz, 1H, *ArH*), 7.93 – 7.90 (m, 1H, *ArH*), 7.88 (d, *J* = 8.7 Hz, 1H, *ArH*), 7.75 – 7.65 (m, 3H, *ArH*), 7.37 (d, *J* = 8.2 Hz, 1H, *ArH*), 7.29 (m, 1H, *ArH*), 7.24 (m, 1H, *ArH*), 7.16 (ddd, *J* = 8.2, 4.7, 3.5 Hz, 1H, *ArH*), 6.79 (s, 1H, *NCHC*), 6.78 (t, *J* = 1.1 Hz, 1H, *ArH*), 3.93 (s, 3H, *NCH*₃). **¹³C NMR** (101 MHz, CDCl₃) δ 147.0, 146.8, 137.0, 135.4, 135.3, 133.9, 132.8, 129.7, 128.5, 128.4, 127.8, 127.5, 127.4, 127.1, 126.2,

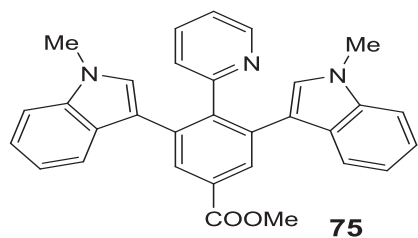
125.7, 121.0, 120.8, 120.7, 118.5, 108.9, 32.9. **HR-ESI-MS** 309.1398 ($[M+H]^+$, $C_{22}H_{17}N_2^+$; calc. for 309.1386).

1'-Methyl-1-(pyrimidin-2-yl)-1*H*,1'*H*-2,3'-biindole (**74**)



Starting from 1-(pyrimidin-2-yl)-1*H*-indole **123** (59.0 mg, 0.300 mmol) and with 1-(3-1-methyl-1*H*-indole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, 1'-methyl-1-(pyrimidin-2-yl)-1*H*,1'*H*-2,3'-biindole **74** (80.0 mg, 0.247 mmol, 82% yield) was obtained as a yellow oil. **Rf**: 0.38 (Pentane:EtOAc 4:1). **IR** ν 3049 (w), 2931 (w), 1592 (w), 1563 (m), 1454 (m), 1423 (s), 1372 (w), 1350 (w), 1309 (m), 1258 (w), 1217 (w), 910 (w). **¹H NMR** (400 MHz, $CDCl_3$) δ 8.51 (d, J = 4.8 Hz, 2H, Ar*H*), 8.01 (m, 1H, Ar*H*), 7.56 (dd, J = 7.9, 1.3 Hz, 1H, Ar*H*), 7.22 – 7.14 (m, 3H, Ar*H*), 7.13 (s, 1H, Ar*H*), 7.06 (dd, J = 8.3, 6.9 Hz, 2H, Ar*H*), 6.93 (t, J = 4.8 Hz, 1H, Ar*H*), 6.82 (td, J = 7.4, 0.9 Hz, 1H, Ar*H*), 6.69 (s, 1H, CH_3NCHC), 3.71 (s, 3H, NCH_3). **¹³C NMR** (101 MHz, $CDCl_3$) δ 158.2, 158.2, 137.5, 136.8, 134.6, 129.6, 127.8, 126.8, 122.6, 121.8, 121.7, 120.0, 119.8, 119.5, 117.5, 112.4, 109.3, 108.9, 106.5, 32.9. **HR-ESI-MS** 325.1452 ($[M+H]^+$, $C_{21}H_{17}N_4^+$; calc. for 325.1448).

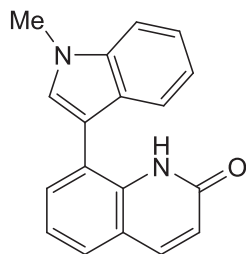
Methyl 3,5-bis(1-methyl-1*H*-indol-3-yl)-4-(pyridin-2-yl)benzoate (**75**)



Starting from methyl 4-(pyridin-2-yl)benzoate **121** (64.0 mg, 0.300 mmol) and with 1-(3-1-methyl-1*H*-indole)-1*H*-1*λ*₃-benzo[*b*]iodo-3(2*H*)-one **21** (249 mg, 0.660 mmol, 2.20 equiv.) at 50 °C, methyl 3,5-bis(1-methyl-1*H*-indol-3-yl)-4-(pyridin-2-yl)benzoate **75** (75.0 mg, 0.159 mmol, 53% yield) was obtained as a yellow oil. **Rf**: 0.30 (Pentane:EtOAc 4:1). **IR** ν 3056 (w), 2950 (w), 2247 (w), 1720 (m), 1571 (m), 1477 (m), 1427 (m), 1325 (m), 1293 (s), 1247 (s), 1161 (m), 1119 (m), 1004 (m), 908 (s). **¹H NMR** (400 MHz, $CDCl_3$) δ 8.47 (m, 1H, Ar*H*), 8.32 (s, 2H, Ar*H*), 7.68 (d, J = 8.0 Hz, 2H, Ar*H*), 7.29 – 7.15 (m, 5H, Ar*H*), 7.08 (ddd, J = 8.2, 6.5, 1.5 Hz, 2H, Ar*H*), 6.99 – 6.93 (m, 2H, Ar*H*), 6.52 (s, 2H, Ar*H*), 3.94 (s, 3H, $COOMe$), 3.58 (s, 6H, NMe). **¹³C NMR** (101 MHz, $CDCl_3$) δ 167.2, 159.8, 147.9, 143.2, 136.4, 135.6, 135.4, 129.7, 128.9, 127.3,

125.7, 121.6, 121.5, 119.8, 119.5, 114.5, 109.0, 52.1, 32.6. **HR-ESI-MS** 472.2021 ($[M+H]^+$, $C_{31}H_{25}N_3O_2^+$; calc. for 472.1998).

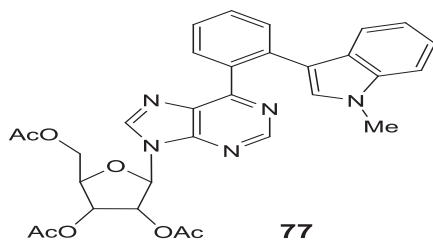
8-(1-Methyl-1*H*-indol-3-yl)quinolin-2(1*H*)-one (76)



76

Starting from commercially available quinoline 1-oxide (44.0 mg, 0.300 mmol) and with 1-(3-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 100 °C, 8-(1-methyl-1*H*-indol-3-yl)quinolin-2(1*H*)-one **76** (31.0 mg, 0.113 mmol, 38% yield) was obtained as a yellow oil. **Rf**: 0.58 (EtOAc:MeOH 10:1). **IR** ν 3367 (w), 3053 (w), 2923 (m), 2853 (w), 1715 (w), 1651 (s), 1608 (m), 1541 (w), 1467 (m), 1372 (w), 1333 (w), 1234 (w), 1135 (w), 1014 (w), 840 (m). **¹H NMR** (400 MHz, CDCl₃) δ 9.02 (s, 1H, *NHCO*), 7.83 (d, *J* = 9.5 Hz, 1H, *ArH*), 7.61 – 7.54 (m, 2H, *ArH*), 7.45 (dd, *J* = 8.3, 6.7 Hz, 2H, *ArH*), 7.34 (m, 1H, *ArH*), 7.30 (d, *J* = 7.6 Hz, 1H, *ArH*), 7.23 (s, 1H, *NCHC*), 7.20 – 7.15 (m, 1H, *IndoleH*), 6.66 (d, *J* = 9.3 Hz, 1H, *ArH*), 3.91 (s, 3H, *NCH₃*). **¹³C NMR** (101 MHz, CDCl₃) δ 162.4, 141.0, 136.3, 132.2, 127.8, 127.7, 126.9, 126.7, 122.9, 122.4, 121.9, 121.6, 120.6, 120.0, 119.4, 109.8, 109.4, 33.1. **HR-ESI-MS** 275.1185 ($[M+H]^+$, $C_{18}H_{15}N_2O^+$; calc. for 275.1179).

(2*R*,3*R*,4*R*,5*R*)-2-(Acetoxymethyl)-5-(6-(2-(1-methyl-1*H*-indol-3-yl)phenyl)-9*H*-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate (77)



77

Starting from (2*R*,3*R*,4*R*,5*R*)-2-(acetoxymethyl)-5-(6-phenyl-9*H*-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate **127** (136 mg, 0.300 mmol) and with 1-(3-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **21** (124 mg, 0.330 mmol, 1.10 equiv.) at 50 °C, (2*R*,3*R*,4*R*,5*R*)-2-(Acetoxymethyl)-5-(6-(2-(1-methyl-1*H*-indol-3-yl)phenyl)-9*H*-purin-9-yl)tetrahydrofuran-3,4-diyl diacetate **77** (72 mg, 0.123 mmol, 41% yield) was obtained as a yellow oil. **Rf**: 0.65 (EtOAc 100%). **IR** ν 3056 (w), 2934 (w), 2825 (w), 2254 (w), 1749 (s), 1586 (m), 1505 (w), 1484 (w), 1435 (w), 1377 (m), 1332 (m), 1219 (s), 1101 (m), 1048 (m), 912 (m), 817 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.81 (s, 1H, *ArH*), 8.04 (s, 1H, *ArH*), 7.76 (dd, *J* = 7.6, 1.4 Hz, 1H, *ArH*), 7.70 (dd,

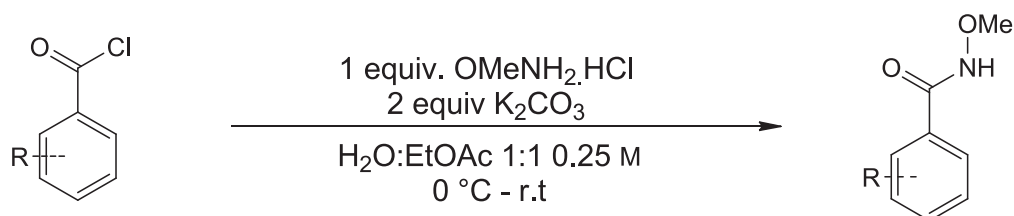
$J = 7.6, 1.3$ Hz, 1H, ArH), 7.56 (td, $J = 7.6, 1.5$ Hz, 1H, ArH), 7.46 (td, $J = 7.5, 1.3$ Hz, 1H, ArH), 7.30 – 7.23 (m, 1H, ArH + $CDCl_3$), 7.18 (d, $J = 8.3$ Hz, 1H, ArH), 7.08 (ddd, $J = 8.1, 7.0, 1.1$ Hz, 1H, ArH), 6.90 (s, 1H, ArH), 6.86 (ddd, $J = 8.0, 6.9, 1.0$ Hz, 1H, ArH), 6.18 (d, $J = 5.1$ Hz, 1H, CH), 5.89 (t, $J = 5.3$ Hz, 1H, CH), 5.65 (dd, $J = 5.5, 4.5$ Hz, 1H, CH), 4.47 – 4.40 (m, 2H, CH + CH_2), 4.34 (dd, $J = 13.1, 5.2$ Hz, 1H, CH_2), 3.67 (s, 3H, NMe), 2.14 (s, 3H, $COCH_3$), 2.08 (s, 3H, $COCH_3$), 2.06 (s, 3H, $COCH_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.3, 169.5, 169.2, 160.3, 152.3, 151.0, 142.4, 136.6, 134.7, 134.2, 132.9, 131.3, 131.0, 129.8, 128.2, 126.9, 126.2, 121.4, 119.5, 119.2, 115.4, 109.0, 86.3, 80.2, 73.0, 70.5, 62.9, 32.7, 20.7, 20.5, 20.4. **HR-ESI-MS** 584.2138 ($[M+H]^+$, $C_{31}H_{30}N_5O_7^+$; calc. for 584.2140).

4. Ru-Catalyzed C-H Indolization of Arenes *via* C-H activation.

All commercially available chemicals were purchased from the suppliers quoted in Paragraph 1.0 of Supplementary Informations: these chemicals were purified through a short plug of celite prior to their use in catalysis. The synthesis of non commercial available compounds is presented below.

The synthesis of the starting materials **14**, **53-62** the optimization process of compound **79** and products **79**, **85-94** had been already described before.^[1] The procedures here reported are taken from the cited publication to facilitate reproduction of the results by having all the data in the same file.

4.1 Preparation of starting materials for Ru-Catalyzed C-H activation.



GP5: Following a reported procedure,^[35] O-methylhydroxylamine hydrochloride (0.418 g, 5.00 mmol, 1.00 equiv.) was added to a solution of K₂CO₃ (1.38 g, 10.0 mmol, 2.00 equiv) in a mixture of EtOAc/H₂O (20 mL, 1:1 0.25 M) under vigorous stirring. Then the reaction mixture was cooled to 0 °C and the corresponding (substituted) benzoyl chloride (5.00 mmol, 1.00 equiv) was added dropwise or portionwise. The reaction mixture was warmed to room temperature and stirred for additional 2 hours. The organic layer was separated and the aqueous layer was extracted with EtOAc (3x10 mL). The combined organic layers were dried over MgSO₄, filtered, and the solvent removed under reduced pressure. The crude product was purified by flash column chromatography (Pentane:EtOAc 2:1) to afford the desired N-methoxy benzamides **78**, **129-138**.

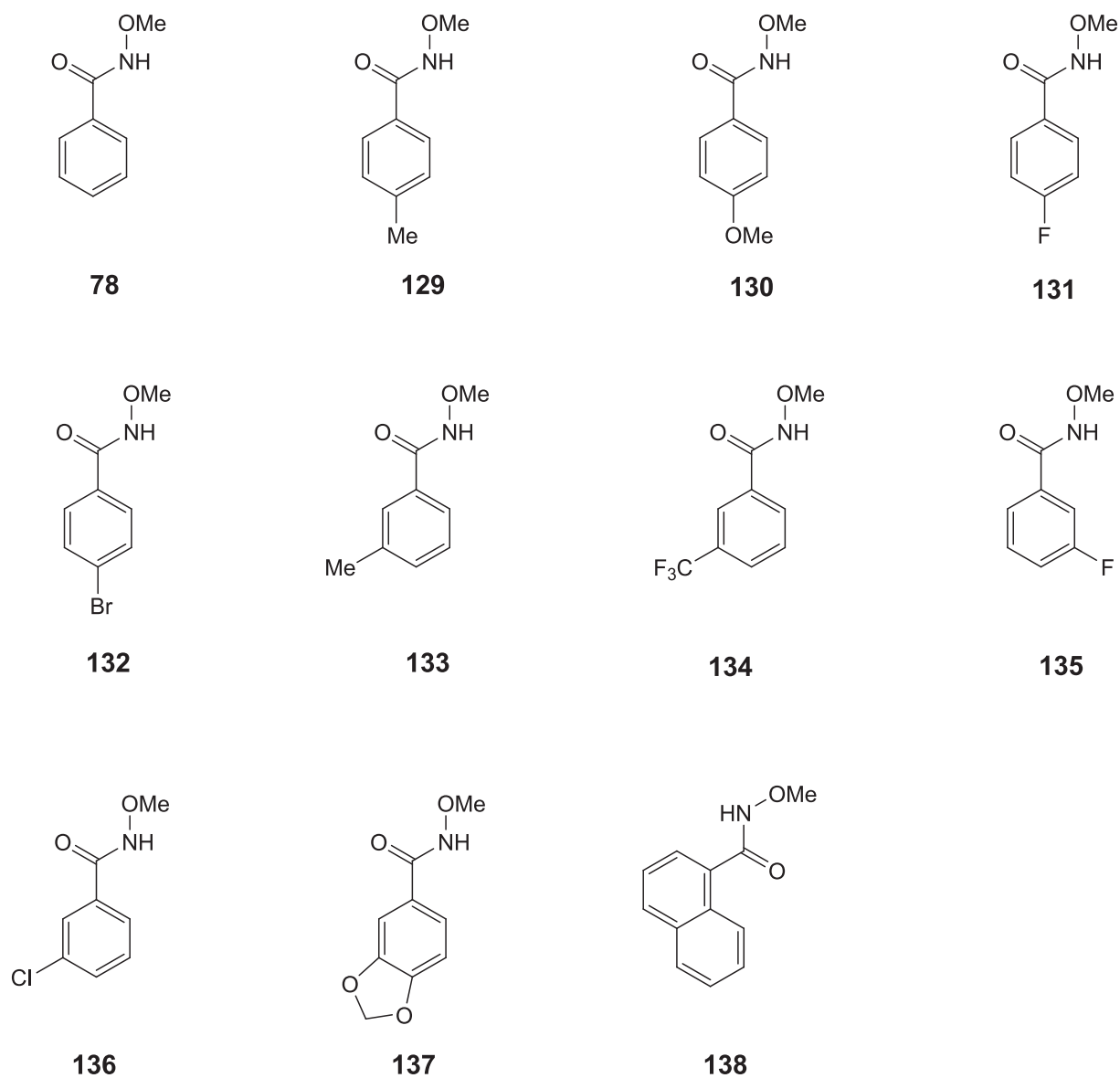
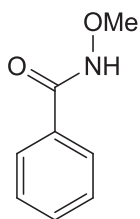


Figure S10: Starting materials for Ru-catalyzed Indolization of Arenes via C-H activation..

N-Methoxybenzamide (78)

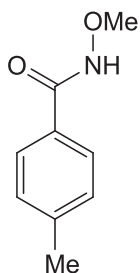


78

The synthesis of N-methoxybenzamide **14** was scaled up to 10 mmol without reoptimization of the protocol.

Starting from commercially available benzoyl chloride (1.15 mL, 10.0 mmol), N-methoxybenzamide **78** (1.20 g, 7.94 mmol, 79% yield) was obtained as a colorless solid. **IR** ν 3197 (w), 2980 (w), 2935 (w), 1646 (s), 1579 (m), 1516 (m), 1484 (m), 1310 (m), 1154 (w), 1045 (m), 1026 (m), 945 (w), 881 (s). **^1H NMR** (400 MHz, CDCl_3) δ 10.70 (s, 1H, NHOCCH_3), 7.70 (dd, $J = 8.3, 1.4$ Hz, 2H, ArH), 7.38 (m, 1H, ArH), 7.26 (ddd, $J = 8.3, 6.6, 1.3$ Hz, 2H, ArH), 3.69 (s, 3H, NHOCCH_3). **^{13}C NMR** (100 MHz, CDCl_3) δ 166.2, 131.7, 128.3, 127.1, 63.9, 53.3. NMR values are in accordance with the data reported in literature.^[34]

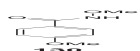
N-Methoxy-4-methylbenzamide (129)



129

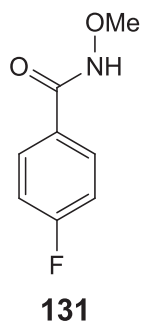
Starting from commercially available 4-methylbenzoyl chloride (775 mg, 5.00 mmol), N-methoxy-4-methylbenzamide **129** (822 mg, 4.98 mmol, 100% yield) was obtained as a colorless solid. **IR** ν 3201 (w), 2975 (w), 2935 (w), 1646 (s), 1572 (w), 1494 (m), 1439 (w), 1308 (m), 1155 (w), 1043 (s), 1020 (m), 943 (w), 883 (s), 833 (m). **^1H NMR** (400 MHz, CDCl_3) δ 10.73 (brs, 1H, NHOCCH_3), 7.67 (d, $J = 8.2$ Hz, 2H, ArH), 7.10 (d, $J = 8.0$ Hz, 2H, ArH), 3.74 (s, 3H, NHOCCH_3), 2.30 (s, 3H, ArCH_3). **^{13}C NMR** (100 MHz, CDCl_3) δ (ppm) 166.2, 142.1, 128.9, 127.1, 63.8, 21.2 (2 aromatic Carbon signals overlapping at 128.9). NMR values are in accordance with the data reported in literature.^[34]

N,4-dimethoxybenzamide (130)



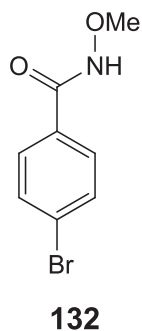
Starting from commercially available 4-methoxybenzoyl chloride (853 mg, 5.00 mmol), 4-fluoro- N,4-dimethoxybenzamide **130** (890 mg, 4.91 mmol, 98% yield) was obtained as a white solid. **IR** ν 3205 (w), 2972 (w), 2938 (w), 1644 (m), 1606 (s), 1496 (m), 1255 (s), 1181 (m), 1159 (m), 1027 (s), 884 (m), 844 (m). **^1H NMR** (400 MHz, CDCl_3) δ 10.67 (s, 1H, NHOMe), 7.77 (d, $J = 8.9$ Hz, 2H, ArH), 6.81 (d, $J = 8.4$ Hz, 2H, ArH), 3.77 (s, 3H, NHOMe), 3.76 (s, 3H, ArOMe). **^{13}C NMR** (100 MHz, CDCl_3) δ 162.2, 132.6, 128.9, 114.0, 113.5, 63.8, 55.1. NMR values are in accordance with the data reported in literature.^[34]

4-Fluoro-N-methoxybenzamide (131)



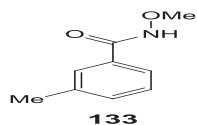
Starting from commercially available 4-fluorobenzoyl chloride (793 mg, 5.00 mmol), 4-fluoro-N-methoxybenzamide **131** (643 mg, 3.80 mmol, 76% yield) was obtained as a colorless solid. **IR** ν 3210 (w), 2984 (w), 2941 (w), 1656 (s), 1592 (s), 1481 (s), 1439 (w), 1318 (w), 1154 (w), 1072 (s), 1012 (s), 944 (w), 879 (s), 841 (m). **¹H NMR** (400 MHz, CDCl₃) δ 11.29 (s, 1H, NHOMe), 7.78 (m, 2H, ArH), 6.96 (m, 2H, ArH), 3.72 (s, 3H, NHOMe). **¹³C NMR** (101 MHz, CDCl₃) 165.2, 164.7 (d, J = 252.5 Hz), 129.6 (d, J = 9.0 Hz), 127.6 (d, J = 3.3 Hz), 115.3 (d, J = 22.0 Hz), 63.7. NMR data is corresponding to the reported values.^[34]

4-Bromo-N-methoxybenzamide (132)



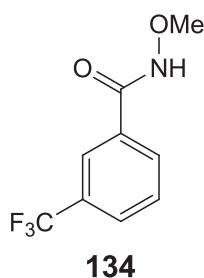
Starting from commercially available 4-bromobenzoyl chloride (1.09 g, 5.00 mmol), 4-bromo-N-methoxybenzamide **132** (700 mg, 3.04 mmol, 61% yield) was obtained as a colorless solid. **IR** ν 3059 (w), 3006 (w), 1647 (s), 1604 (s), 1497 (s), 1267 (s), 1237 (s), 1158 (m), 1041 (m), 885 (m), 850 (s). **¹H NMR** (400 MHz, CDCl₃) δ 10.59 (brs, 1H, NHOCH₃), 7.56 (d, J = 8.5 Hz, 2H, ArH), 7.41 (d, J = 8.6 Hz, 2H), 3.71 (s, 3H, NHOCH₃). **¹³C NMR** (100 MHz, CDCl₃) δ 165.4, 131.7, 130.4, 128.8, 126.7, 64.1. ¹H NMR data is corresponding to the reported values.^[34]

N-Methoxy-3-methylbenzamide (133)



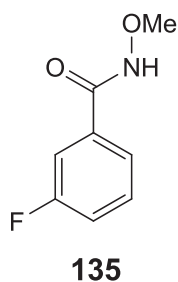
Starting from commercially available 3-methylbenzoyl chloride (775 mg, 5.00 mmol), N-methoxy-3-methylbenzamide **133** (813 mg, 4.92 mmol, 98% yield) was obtained as a white solid. **IR** ν 3004 (w), 2953 (w), 1726 (s), 1650 (m), 1516 (w), 1439 (m), 1303 (m), 1264 (s), 1156 (m), 1109 (w), 982 (w), 826 (w). **¹H NMR** (400 MHz, CDCl₃) δ (ppm) 11.09 (s, 1H, NHOCH₃), 8.37 (s, 1H, ArH), 8.03 (dt, J = 7.8, 1.5 Hz, 1H), 7.98 (dt, J = 7.8, 1.5 Hz, 1H), 7.39 (t, J = 7.8 Hz, 1H), 3.78 (s, 6H, NHOMe + ArCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 166.0, 132.4, 132.0, 131.6, 130.1, 128.5, 128.1, 63.9, 52.1. NMR values are in accordance with the data reported in literature.^[34]

N-Methoxy-3-(trifluoromethyl)benzamide (134)



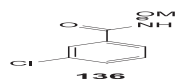
Starting from commercially available 3-(trifluoromethyl)benzoyl chloride (1.04 g, 5.00 mmol), N-methoxy-4-methylbenzamide **134** (822 mg, 3.75 mmol, 75% yield) was obtained as a colorless solid. **IR** ν 3190 (w), 2995 (w), 1656 (m), 1522 (w), 1440 (w), 1330 (s), 1283 (m), 1169 (s), 1125 (s), 1075 (m), 909 (w). **¹H NMR** (400 MHz, CDCl₃) δ 9.60 (s, 1H, *NH*OCH₃), 8.02 (s, 1H, *ArH*), 7.95 (d, *J* = 8.1 Hz, 1H, *ArH*), 7.56 (t, *J* = 7.8 Hz, 1H, *ArH*), 3.87 (s, 3H, *NH*OCH₃). **¹³C NMR** (100 MHz, CDCl₃) δ 168.3, 130.5, 129.3, 128.7, 128.6, 124.2, 124.2, 123.5 (q, *J*_F = 272.6 Hz), 64.6. NMR values are in accordance with the data reported in literature.^[36]

3-Fluoro-N-methoxybenzamide (135)



Starting from commercially available 3-fluorobenzoyl chloride (775 mg, 5.00 mmol), 3-fluoro-N-methoxybenzamide **135**¹ (710 mg, 4.20 mmol, 84% yield) was obtained as a colorless solid. **Mp**: 67.9°C. **IR** 2979 (w), 2940 (w), 1652 (s), 1587 (s), 1519 (m), 1483 (m), 1226 (s), 1046 (m), 937 (m), 816 (s). **¹H NMR** (400 MHz, CDCl₃) δ 10.76 (brs, 1H, *NH*OCH₃), 7.57 (m, 1H, *ArH*), 7.50 (ddd, *J* = 9.4, 2.6, 1.6 Hz, 1H, *ArH*), 7.30 – 7.21 (m, 1H, *ArH*), 7.08 (t, *J* = 8.8 Hz, 1H, *ArH*), 3.73 (s, 3H, *NH*OCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 165.0, 162.4 (d, *J* = 247.6 Hz), 133.7 (d, *J* = 6.9 Hz), 130.1 (d, *J* = 7.8 Hz), 122.8, 118.9 (d, *J* = 21.2 Hz), 114.4 (d, *J* = 23.3 Hz), 64.0. **Mp** and **IR** significant values are in accordance with the data reported in literature.^[37]

3-Chloro-N-methoxybenzamide (136)

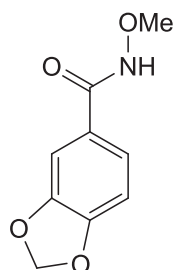


Starting from commercially available 3-chlorobenzoyl chloride (875 g, 5.00 mmol), 3-chloro-N-methoxybenzamide **136** (830 mg, 4.47 mmol, 89% yield) was obtained as a white solid. **IR** ν 3187 (w), 3006 (w), 2937 (w), 1646 (s), 1572 (s), 1519 (m), 1471 (m), 1298 (m), 1162 (m), 1048 (m), 944 (m), 904 (m). **¹H NMR** (400 MHz, CDCl₃): δ 9.90 (br s, 1H, *NH*OCH₃), 7.75 (s, 1H, *ArH*), 7.64 (d, *J* = 7.8 Hz, 1H, *ArH*), 7.45 (dd, *J* = 8.1, 2.1 Hz, 1H, *ArH*), 7.32 (t, *J* = 7.9 Hz, 1H,

1: Compound **59** is purchaseable via Adlab Chemicals Building Blocks and Aurora Building Blocks.

ArH), 3.83 (s, 3H, NHCH_3). ^{13}C NMR (101 MHz, CDCl_3): δ 165.1, 134.7, 133.4, 132.0, 129.9, 127.5, 125.3, 64.4. NMR values are in accordance with the data reported in literature.^[38]

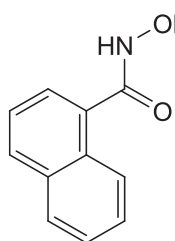
N-Methoxybenzo[d][1,3]dioxole-5-carboxamide (**137**)



137

Starting from commercially available benzo[d][1,3]dioxole-5-carbonyl chloride (923 mg, 5.00 mmol), N-methoxybenzo[d][1,3]dioxole-5-carboxamide **137** (865 mg, 4.43 mmol, 89% yield) was obtained as a white solid. **Rf**: 0.4 (Pentane:EtOAc 4:1). **IR** ν 2982 (w), 2938 (w), 1650 (m), 1605 (m), 1478 (s), 1438 (m), 1300 (m), 1252 (s), 1093 (m), 1034 (s), 927 (s), 839 (m). ^1H NMR (400 MHz, CDCl_3) δ 10.59 (br s, 1H, NHCH_3), 7.31 (d, J = 8.2, 1.8 Hz, 1H, ArH), 7.23 (s, 1H, ArH), 6.69 (d, J = 8.1, Hz, 1H, ArH), 5.92 (s, 2H, OCH_2O), 3.75 (s, 3H, NHCH_3). ^{13}C NMR (101 MHz, CDCl_3) δ 165.7, 150.4, 147.6, 125.5, 122.1, 107.8, 107.5, 101.5, 63.9. **HR-ESI-MS** 196.0604 ($[\text{M}+\text{H}]^+$, $\text{C}_9\text{H}_{10}\text{NO}_4^+$; calc. for 196.0604).

N-Methoxy-1-naphthamide (**138**)



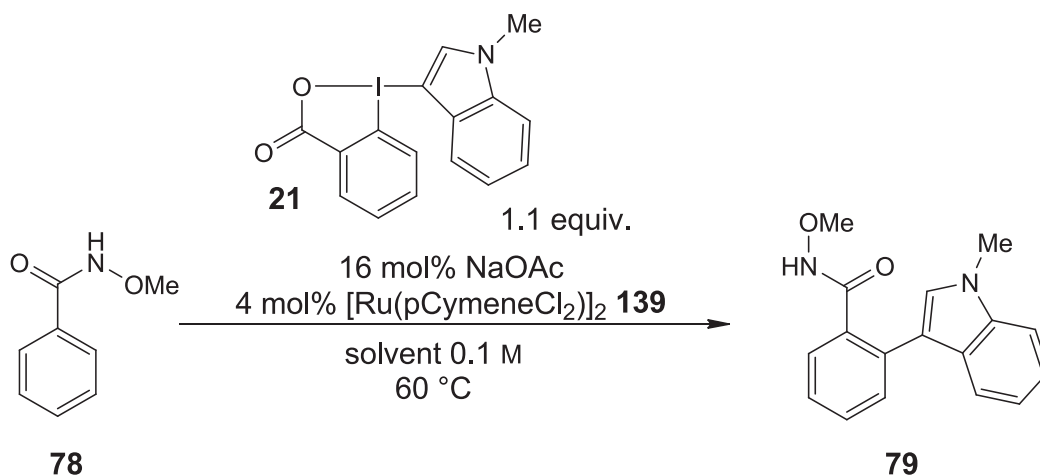
138

For this starting material the synthesis was performed on 1.00 mmol scale
Starting from commercially available 1-naphthoyl chloride (191 mg, 1.00 mmol), N-methoxy-1-naphthamide **138** (183 mg, 0.909 mmol, 91% yield) was obtained as a white solid. **IR** 2943 (w), 2907 (w), 2827 (w), 1631 (s), 1617 (s), 1591 (m), 1537 (w), 1318 (w), 1262 (w), 1063 (m), 958 (m), 889 (w). ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 8.72 (br s, 1H, NHCH_3), 8.28 (m, 1H, ArH), 8.10–7.90 (m, 2H, ArH), 7.71–7.41 (m, 4H, ArH), 3.94 (s, 3H, NHCH_3). ^{13}C NMR (75 MHz, CDCl_3) δ 167.3, 133.6, 131.4, 130.3, 129.6, 128.3, 127.4, 126.6, 125.6, 125.1, 124.5, 64.8. NMR values are in accordance with the data reported in literature.^[39]

4.2 Optimization of the Ru-Catalyzed Indolization of Arenes via C-H activation.

GP5: In a vial, N-methoxybenzamide **78** (15.0 mg, 0.100 mmol), 1-(3-1-methyl-1*H*-indole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one **21** (1.10 equiv.), [RuCl₂(*p*-cymene)]₂ **139** (2.45 mg, 4.00 μmol, 4 mol%) and the relative additives (16 mol%) were dissolved in the specified dry solvent (0.1 M) under nitrogen. the reaction mixture was degassed (freeze-thaw-pump) and stirred at the reported T in °C overnight. Then the reaction was stopped, the organic layer washed with a saturated solution of NaHCO₃ (2 ml) and the solvent removed under reduced pressure. Flash column chromatography (Pentane:EtOAc 2:1) afforded the desired product (*see compound 79's characterization for all the chemical data*).

Table S9: Screening of solvents

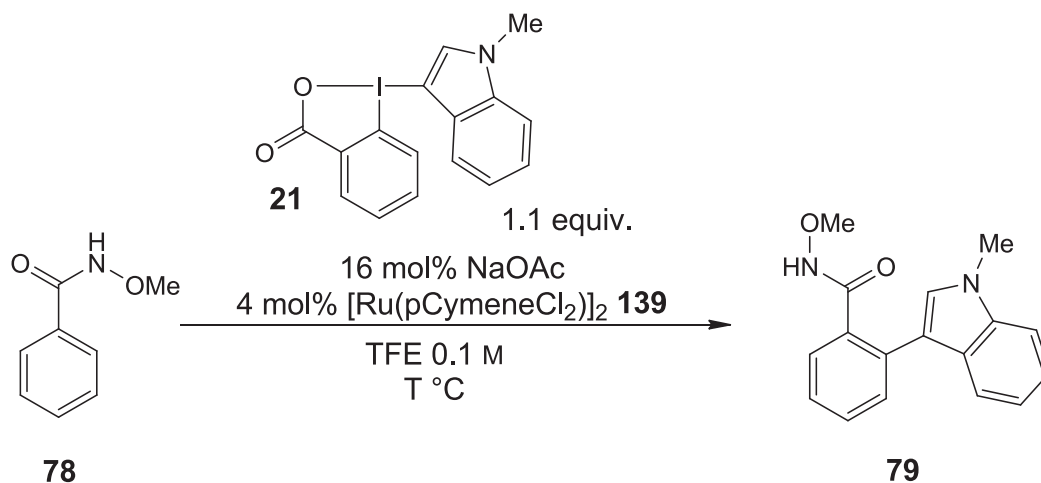


Entry	Solvent	Yield% ^a
1	DCM	-
2	DCE	-
3	MeOH	43%
4	EtOH	34%
5	<i>t</i> -BuOH	-
6	<i>t</i> -AmylOH	-
7	Toluene	-
8	Xylene	-
9	Dioxane	28%

10	MeCN	-
11	DMF	-
12	2,2,2-Trifluoroethanol (TFE)	55%
13	Hexafluoroisopropanol (HFIP)	30%
14	Nonafluoroisopropanol (NFIP):HFIP 1:9	-
15	HFIP:DCE 9:1	-
16	HFIP:DCE 8:2	35%
17	HFIP:DCE 1:1	-
18	Monofluoroethanol (MFE)	21%

a) Substrate **78** (0.100 mmol), IndoleBX **21** (0.110 mmol), [Ru(pCymeneCl₂)₂] **139** (4 mol%), NaOAc (16 mol%) and **solvent** (0.1 M) at 60 °C. Isolated yield after flash chromatography is given.

Table S10: Screening of the Temperature

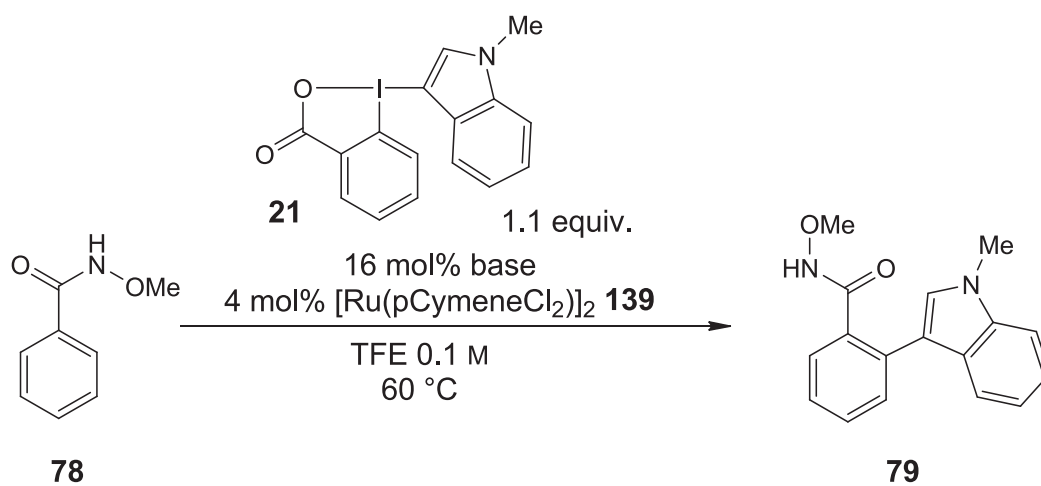


Entry	T	Yield% ^a
1	r.t	- ^b
2	40	low conversion ^b
3	60	55%
4	80	low conversion ^c
5	120	- ^c

a) Substrate **78** (0.100 mmol), IndoleBX **21** (0.110 mmol), [Ru(pCymeneCl₂)₂] **139** (4 mol%), NaOAc (16 mol%) and TFE (0.1 M) at T

°C. Isolated yield after flash chromatography is given. b) clean reaction, starting material recovered. c) decomposition occurred.

Table S11: Screening of the base



Entry	Base	Yield% ^a
1	LiOPiv	-
2	Li ₂ CO ₃	-
3	LiMes	- ^b
4	NaOAc	55%
5	Na ₂ CO ₃	-
6	NaOPiv	50%
7	NaMes	34%
8	63	- ^b
9	64	68%^c
10	65	65% ^b
11	66	66% ^b
12	KOAc	-
13	KOPiv	-
14	KMes	26% ^b
15	CsOPiv	-
16	Cs ₂ CO ₃	-

a) Substrate **78** (0.100 mmol), IndoleBX **21** (0.110 mmol), [Ru(pCymeneCl₂)₂] **139** (4 mol%), **base** (16 mol%) and TFE (0.1 M) at 60 °C. Isolated yield after flash chromatography is given. b) decomposition occurred. c) clean reaction, starting material recovered.

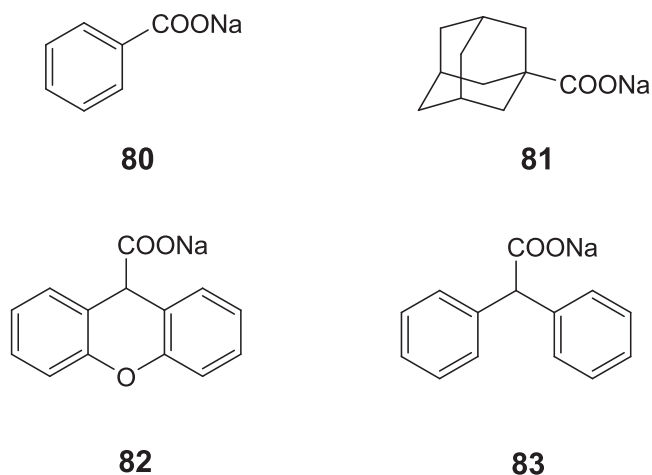
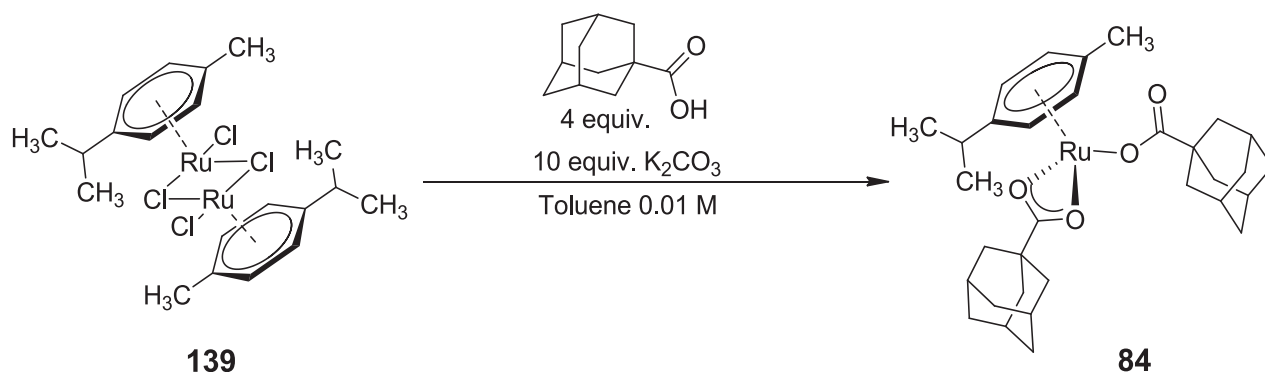


Table S12: Screening of the silver(I) additive

Entry	Solvent	Yield % ^a
1	none	68% ^c
2	Ag(NTf ₂)	– ^b
3	AgSbF ₆	– ^c
4	AgPF ₆	– ^b
5	AgBF ₄	– ^b
6	AgOTf	– ^b
7	AgOTs	– ^b
8	AgOAc	– ^c
9	AgBenzoate	– ^b
10	AgTFA	– ^c

a) Substrate **78** (0.100 mmol), IndoleBX **21** (0.110 mmol), [Ru(pCymeneCl₂)₂] **139** (4 mol%), NaCOOAd (16 mol%), **silver(I) additive** (16 mol%) and TFE (0.1 M) at 60 °C. Isolated yield after flash chromatography is given. b) decomposition occurred. c) clean reaction, starting material recovered.

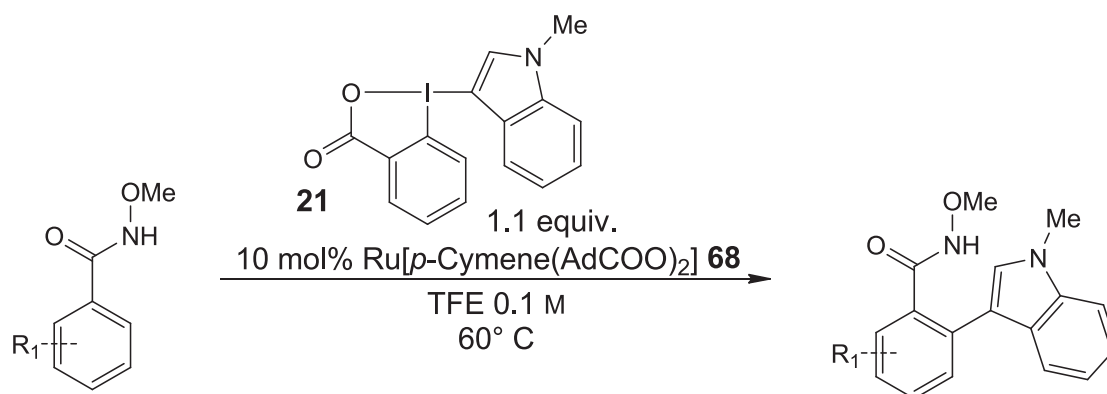
4.3 Preparation of the Ruthenium Catalyst (**84**).



Following a reported procedure,² [RuCl₂(p-cymene)]₂ **139** (105 mg, 0.163 mmol), adamantane-1-carboxylic acid (118 mg, 0.652 mmol, 4.00 equiv.) and K₂CO₃ (225 mg, 1.63 mmol, 10.0 equiv.) were suspended in toluene (16.0 mL, 0.01 M) under N₂. The resulting suspension was stirred for 3 hours at r.t.. The solvent was then removed *in vacuo* and the residue dissolved in dry CH₂Cl₂ (20 mL). The resulting suspension was filtered under N₂ through a short plug of celite. The solvent was removed *in vacuo* to yield (catalyst) complex **84** (90.0 mg, 0.156 mmol, 96% yield) as an orange solid. ¹H NMR (300 MHz, CDCl₃): δ 5.70 (d, *J* = 5.7 Hz, 2H, ArH), 5.49 (d, *J* = 5.7 Hz, 2H, ArH), 2.88 (hept, *J* = 7.1 Hz, 1H, ArCH(CH₃)₂), 2.23 (s, 3H, ArCH₃), 1.92 (t, *J* = 3.3 Hz, 6H, ArCH(CH₃)₂), 1.78 (s, 12H, AdCH₂), 1.63 (s, 12H, AdCH₂), 1.33 (d, *J* = 6.9 Hz, 6H, AdCH). ¹H-NMR values are in accordance with the data reported in literature.³⁵

[2] L. Ackermann, P. Novák, R. Vicente, N. Hofmann, *Angew. Chem. Int. Ed.* **2009**, 48, 6045–6048.

4.4 Scope of the Ru-Catalyzed Indolization via C-H activation.



GP6: In a vial, freshly synthesized benzamide **78**, **129-138** (50.0 mg, 0.300 mmol), 1-(3-(1-methyl-1H-indol-1-yl)-1H-1,2,3-benzodioxol-3-yl)-1H-1,2,3-benzodioxol-3-one **21** (0.330 mmol, 1.10 equiv.) and freshly synthesized Ruthenium complex **139** (18.2 mg, 30.0 μ mol, 10 mol%), were dissolved in dry TFE (3 ml, 0.1 M) under nitrogen. the reaction mixture was degassed (freeze-thaw-pump) and stirred at 60 °C overnight. It was then allowed to cool down to r.t., washed with a saturated aqueous NaHCO_3 (2ml) and concentrated under reduced pressure. Flash column chromatography (Pentane:EtOAc) afforded the desired products **85-95**.

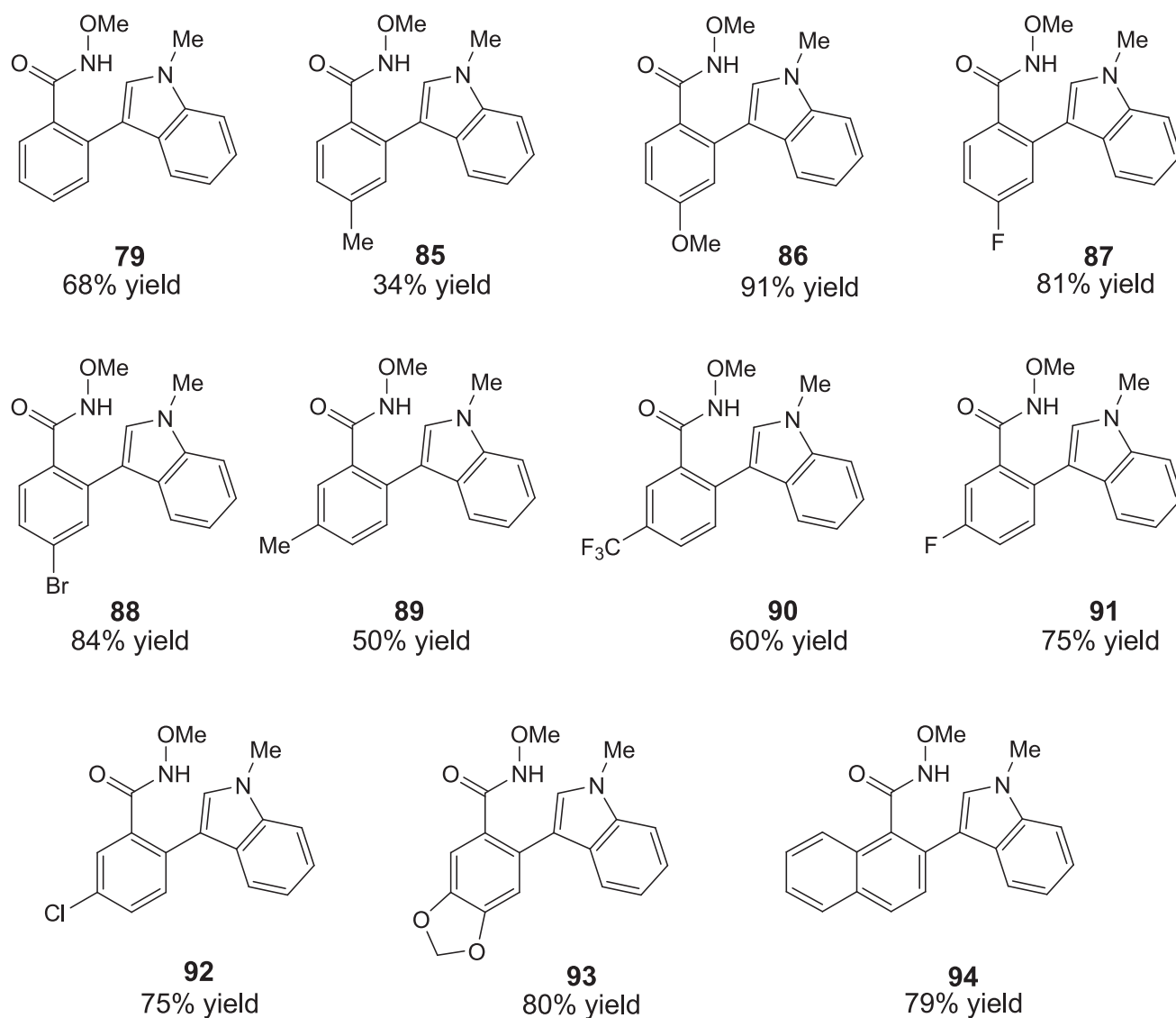


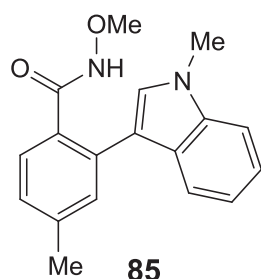
Figure S11: Scope with Methoxy-amides.

N-Methoxy-2-(1-methyl-1H-indol-3-yl)benzamide (79)

Starting from N-methoxybenzamide **78** (45.3 mg, 0.300 mmol), N-methoxy-2-(1-methyl-1H-indol-3-yl)benzamide **79** (57.0 mg, 0.203 mmol, 68% yield) was obtained as a yellow oil. **Rf:** 0.4 (Pentane:EtOAc 2:1). **IR** ν 3209 (w), 3057 (w), 2968 (w), 2934 (m), 2816 (w), 1655 (s), 1599 (w), 1547 (w), 1482 (s), 1464 (m), 1378 (m), 1329 (m), 1223 (m), 1161 (w), 1034 (m), 944 (m), 885 (m). **¹H NMR** (400 MHz, CDCl₃) δ 7.98 (br s, 1H,

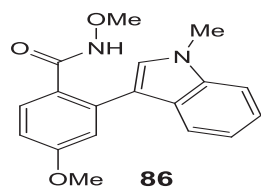
NHOCH₃), 7.74 (dd, $J = 7.5, 5.9$ Hz, 1H, ArH), 7.67 (d, $J = 7.9$ Hz, 1H, IndoleH), 7.57 (dd, $J = 7.8, 1.4$ Hz, 1H, ArH), 7.52 (td, $J = 7.5, 1.4$ Hz, 1H, ArH), 7.38 (m, 2H, ArH + IndoleH), 7.30 (ddd, $J = 8.2, 6.9, 1.1$ Hz, 1H, IndoleH), 7.24 (s, 1H, CH₃NCHC), 7.18 (ddd, $J = 7.9, 6.9, 1.0$ Hz, 1H, IndoleH), 3.85 (s, 3H, NCH₃), 3.46 (s, 3H, NHOCH₃). ¹³C NMR (101 MHz, CDCl₃) δ 168.4, 137.0, 132.5, 132.4, 130.8, 130.7, 129.5, 128.1, 126.8, 126.7, 122.5, 120.3, 119.5, 113.5, 109.6, 63.9, 33.0. **HR-ESI-MS** 303.1108 ([M+Na]⁺, C₁₇H₁₆N₂NaO₂⁺; calc. for 303.1104).

N-Methoxy-4-methyl-2-(1-methyl-1H-indol-3-yl)benzamide (85)



Starting from N-methoxy-4-methylbenzamide **129** (50.0 mg, 0.300 mmol), N-methoxy-4-methyl-2-(1-methyl-1H-indol-3-yl)benzamide **85** (30.0 mg, 0.102 mmol, 34% yield) was obtained as a yellow oil. **Rf**: 0.44 (Pentane:EtOAc 2:1). **IR** ν 3200 (w), 3047 (w), 2936 (w), 1662 (s), 1615 (m), 1543 (w), 1482 (m), 1370 (w), 1331 (w), 1232 (w), 1160 (w), 1086 (w), 1040 (w), 1015 (w), 912 (w), 887 (w), 834 (w). ¹H NMR (400 MHz, CDCl₃) δ 7.97 (br s, 1H, NHOCH₃), 7.71 – 7.64 (m, 2H, ArH), 7.40 – 7.34 (m, 2H, ArH), 7.30 (ddd, $J = 8.2, 6.9, 1.2$ Hz, 1H, ArH), 7.22 – 7.16 (m, 3H, ArH), 3.85 (s, 3H, NCH₃), 3.44 (s, 3H, NHOCH₃), 2.42 (s, 3H, ArCH₃). ¹³C NMR (101 MHz, CDCl₃) δ 168.5, 141.1, 137.0, 132.4, 131.4, 129.7, 129.6, 128.0, 127.7, 126.8, 122.5, 120.4, 119.6, 113.8, 109.6, 63.8, 33.0, 21.5. **HR-ESI-MS** 317.1264 ([M+Na]⁺, C₁₈H₁₈N₂NaO₂⁺; calc. for 317.1260).

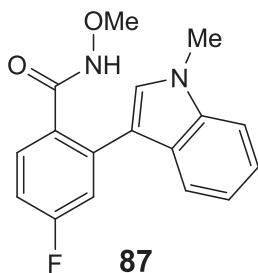
N,4-Dimethoxy-2-(1-methyl-1H-indol-3-yl)benzamide (86)



Starting from N,4-dimethoxybenzamide **130** (54.5 mg, 0.300 mmol), N,4-dimethoxy-2-(1-methyl-1H-indol-3-yl)benzamide **86** (85.0 mg, 0.274 mmol, 91% yield) was obtained as a yellow oil. **Rf**: 0.48 (Pentane:EtOAc 2:1). **IR** ν 3203 (w), 2961 (w), 2936 (w), 2838 (w), 1661 (s), 1603 (s), 1467 (m), 1330 (m), 1279 (m), 1238 (m), 1214 (m), 1084 (m), 1030 (m), 886 (w). ¹H NMR (400 MHz, CDCl₃) δ 8.02 (br s, 1H, NHOCH₃), 7.75 (d, $J = 8.6$ Hz, 1H, ArH), 7.66 (dd, $J = 8.0, 1.0$ Hz, 1H, ArH), 7.38 (d, $J = 8.3$ Hz, 1H, ArH), 7.30 (ddd, $J = 8.1, 7.0, 1.1$ Hz, 1H, ArH), 7.22 (s, 1H, NCHC), 7.18 (ddd, $J = 8.1, 7.0, 1.1$ Hz, 1H, ArH), 7.03 (d, $J = 2.6$ Hz, 1H, ArH), 6.92 (dd, $J = 8.6, 2.6$ Hz, 1H, ArH), 3.85 (s, 3H, NCH₃), 3.85 (s, 3H, OCH₃), 3.43 (s, 3H, NHOCH₃). ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 161.3, 137.0, 134.3, 131.5, 128.0,

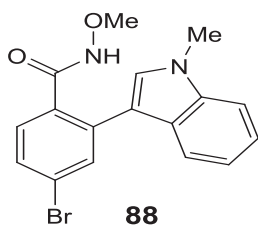
126.7, 124.8, 122.5, 120.4, 119.6, 115.7, 113.7, 112.5, 109.7, 63.8, 55.4, 33.0. **HR-ESI-MS** 333.1210 ($[M+Na]^+$, $C_{18}H_{18}N_2NaO_3^+$; calc. for 333.1210).

5-Fluoro-N-methoxy-2-(1-methyl-1*H*-indol-3-yl)benzamide (**87**)



Starting from 4-fluoro-N-methoxybenzamide **131** (50.7 mg, 0.300 mmol), 4-bromo-N-methoxy-2-(1-methyl-1*H*-indol-3-yl)benzamide **87** (78.0 mg, 0.243 mmol, 81% yield) was obtained as a yellow oil. **Rf**: 0.40 (Pentane:EtOAc 2:1). **IR** ν 3201 (w), 3055 (w), 2984 (w), 2938 (w), 1932 (w), 1663 (m), 1551 (w), 1481 (m), 1455 (m), 1374 (m), 1330 (m), 1266 (s), 1245 (m), 1224 (m), 1161 (w), 1052 (m), 943 (w), 829 (s). **1H NMR** (400 MHz, $CDCl_3$) δ 8.03 (s, 1H, $NHOCH_3$), 7.55 (d, $J = 7.7$ Hz, 1H, *ArH*), 7.48 (m, 1H, *ArH*), 7.42 – 7.35 (m, 2H, *ArH*), 7.33 – 7.27 (m, 2H, *ArH*), 7.23 (s, 1H, $NCHC$), 7.17 (ddd, $J = 8.0, 7.0, 1.1$ Hz, 1H, *ArH*), 3.84 (s, 3H, NCH_3), 3.31 (s, 3H, $NHOCH_3$). **^{13}C NMR** (101 MHz, $CDCl_3$; *two doublet were not resolved*) δ 166.6, 160.1 (d, $J = 247.4$ Hz), 136.8, 135.2, 129.2, 128.6 (d, $J = 8.5$ Hz), 127.1, 125.0, 122.5, 120.4, 119.9 (d, $J = 2.2$ Hz), 118.01 (d, $J = 23.3$ Hz), 109.6, 105.9, 63.6, 33.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -111.7. **HR-ESI-MS** 321.1008 ($[M+Na]^+$, $C_{17}H_{15}FN_2NaO_2^+$; calc. for 321.1010).

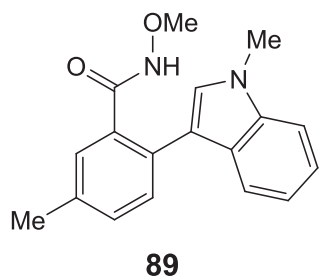
4-Bromo-N-methoxy-2-(1-methyl-1*H*-indol-3-yl)benzamide (**88**)



Starting from 4-bromo-N-methoxybenzamide **132** (69.0 mg, 0.300 mmol), 4-bromo-N-methoxy-2-(1-methyl-1*H*-indol-3-yl)benzamide **88** (91.0 mg, 0.253 mmol, 84% yield) was obtained as an orange oil. **Rf**: 0.35 (Pentane:EtOAc 2:1). **IR** ν 3186 (w), 3063 (w), 2934 (w), 1656 (s), 1605 (s), 1580 (m), 1480 (s), 1364 (w), 1331 (m), 1265 (s), 1195 (m), 1082 (w), 1037 (m), 986 (w), 939 (w), 887 (m), 826 (m). **1H NMR** (400 MHz, $CDCl_3$) δ 8.04 (br s, 1H, $NHOCH_3$), 7.75 (m, 1H, *ArH*), 7.67 (d, $J = 8.0$ Hz, 1H, *ArH*), 7.39 (d, $J = 8.2$ Hz, 1H, *ArH*), 7.33 (m, 1H, *ArH*), 7.28 – 7.24 (m, 2H, *ArH*), 7.21 (m, 1H, *ArH*), 7.07 (td, $J = 8.3, 2.6$ Hz, 1H, *ArH*), 3.85 (s, 3H, NCH_3), 3.46 (s, 3H, $NHOCH_3$). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.4, 137.0, 134.6, 133.3, 131.2, 129.8, 128.4, 126.4, 125.2, 122.8, 120.7, 119.3, 112.3, 109.8, 63.9, 33.1

(one Carbon signal not resolved). **HR-ESI-MS** 381.0204 ($[M+Na]^+$, $C_{17}H_{15}^{79}BrN_2NaO_2^+$; calc. for 381.0209).

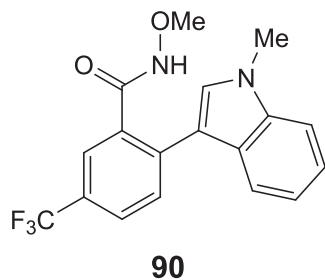
N-Methoxy-5-methyl-2-(1-methyl-1H-indol-3-yl)benzamide (89)



Starting from N-methoxy-3-methylbenzamide **133** (50.0 mg, 0.300 mmol), N-methoxy-5-methyl-2-(1-methyl-1H-indol-3-yl)benzamide **89** (44.0 mg, 0.149 mmol, 50% yield) was obtained as a yellow oil. **Rf**: 0.40 (Pentane:EtOAc 2:1). **IR** ν 3181 (w), 2932 (w), 1713 (s), 1660 (s), 1606 (m), 1538 (w), 1466 (w), 1437 (w), 1289 (m), 1262 (s), 1248 (s), 1162 (w), 1128 (m), 1107 (m), 1038 (w). **¹H NMR** (400 MHz, CD_2Cl_2)

δ 8.27 (s, 1H, ArH), 8.24 (s, 1H, $NHCH_3$), 8.13 (dd, J = 8.1, 1.9 Hz, 1H, ArH), 7.67 (dd, J = 9.9, 8.0 Hz, 2H, ArH), 7.41 (dt, J = 8.3, 0.9 Hz, 1H, ArH), 7.34 (s, 1H, ArH), 7.29 (ddd, J = 8.2, 7.0, 1.1 Hz, 1H, ArH), 7.18 (ddd, J = 8.0, 7.0, 1.1 Hz, 1H, ArH), 3.92 (s, 3H, NCH_3), 3.85 (s, 3H, CH_3), 3.49 (s, 3H, $NHCH_3$). **¹³C NMR** (101 MHz, CD_2Cl_2) δ 166.7, 138.2, 137.8, 133.1, 131.8, 131.2, 131.0, 129.5, 128.6, 127.0, 123.1, 121.0, 119.9, 113.3, 110.4, 64.3, 52.7, 33.6. **HR-ESI-MS** 317.1265 ($[M+Na]^+$, $C_{18}H_{18}N_2NaO_2^+$ calc. for 317.1260).

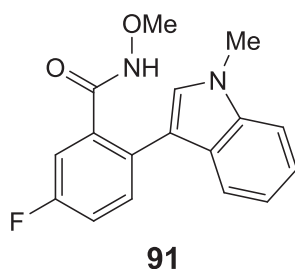
N-Methoxy-2-(1-methyl-1H-indol-3-yl)-5-(trifluoromethyl)benzamide (90)



Starting from N-methoxy-3-(trifluoromethyl)benzamide **134** (65.7 mg, 0.300 mmol), N-methoxy-2-(1-methyl-1H-indol-3-yl)-5-(trifluoromethyl)benzamide **90** (63.0 mg, 0.181 mmol, 60% yield) was obtained as a colorless oil. **Rf**: 0.37 (Pentane:EtOAc 2:1). **IR** ν 3187 (w), 2978 (w), 2935 (w), 1657 (m), 1617 (w), 1549 (w), 1469 (w), 1331 (s), 1274 (w), 1173 (m), 1159 (m), 1127 (s), 1092 (m), 947 (w), 911

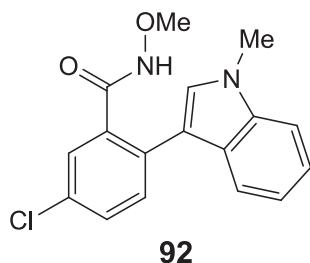
(w), 849 (w). **¹H NMR** (400 MHz, $CDCl_3$) δ 8.00 (br s, 1H, $NHCH_3$), 7.91 (s, 1H, ArH), 7.70 – 7.62 (m, 2H, ArH), 7.59 (d, J = 8.0 Hz, 1H, ArH), 7.33 (m, 1H, ArH), 7.27 (m, 1H, ArH), 7.24 (s, 1H, NCH_3), 7.14 (ddd, J = 8.0, 6.9, 1.1 Hz, 1H, ArH), 3.79 (s, 3H, NCH_3), 3.45 (s, 3H, $NHCH_3$). **¹³C NMR** (101 MHz, $CDCl_3$) δ 167.1, 137.1, 136.4, 132.6, 130.9, 128.8, 128.7, 127.3, 126.7, 126.4, 123.80 (q, J = 272.1 Hz, CF_3), 122.8, 120.8, 119.2, 112.2, 109.9, 64.1, 33.1. **¹⁹F NMR** (376 MHz, $CDCl_3$) δ -62.5. **HR-ESI-MS** 371.0979 ($[M+Na]^+$, $C_{18}H_{15}F_3N_2NaO_2^+$ calc. for 371.0978).

5-Fluoro-N-methoxy-2-(1-methyl-1*H*-indol-3-yl)benzamide (**91**)



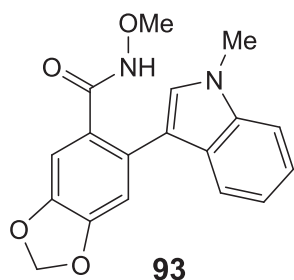
Starting from 3-fluoro-N-methoxybenzamide **135** (50.7 mg, 0.300 mmol), 4-bromo-N-methoxy-2-(1-methyl-1*H*-indol-3-yl)benzamide **91** (84.0 mg, 0.225 mmol, 75% yield) was obtained as a yellow oil. **Rf**: 0.38 (Pentane:EtOAc 2:1). **IR** ν 3179 (w), 3055 (w), 2932 (m), 2853 (w), 1662 (s), 1586 (m), 1550 (w), 1479 (s), 1329 (w), 1256 (w), 1222 (w), 1163 (w), 1089 (m), 1038 (m), 956 (w), 911 (m), 882 (m), 824 (w). **¹H NMR** (400 MHz, CDCl₃) δ 8.00 (br s, 1H, *NH*OCH₃), 7.72 (d, *J* = 2.0 Hz, 1H, *ArH*), 7.64 (t, *J* = 9.1 Hz, 2H, *ArH*), 7.52 (dd, *J* = 8.2, 2.0 Hz, 1H, *ArH*), 7.40 (m, 1H, *ArH*), 7.32 (dd, *J* = 7.0, 1.2 Hz, 1H, *ArH*), 7.25 (s, 1H, *NCHC*), 7.21 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H, *ArH*), 3.85 (s, 3H, *NCH*₃), 3.45 (s, 3H, *NH*OCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 167.6, 163.8 (d, *J* = 250.9 Hz), 137.0, 135.4, 135.3 (d, *J* = 9.4 Hz), 131.8 (d, *J* = 9.5 Hz), 128.4, 128.3, 126.4, 122.7, 120.7, 117.10 (d, *J* = 21.5 Hz), 113.79 (d, *J* = 21.9 Hz), 112.5, 109.8, 63.9, 33.1. **¹⁹F NMR** (376 MHz, CDCl₃) δ -109.3. **HR-ESI-MS** 321.1011 ([*M*+Na]⁺, C₁₇H₁₅FN₂NaO₂⁺ calc. for 321.1010).

5-Chloro-N-methoxy-2-(1-methyl-1*H*-indol-3-yl)benzamide (**92**)



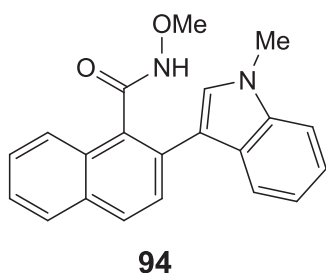
Starting from 3-chloro-N-methoxybenzamide **136** (55.7 mg, 0.300 mmol), N-methoxy-2-(1-methyl-1*H*-indol-3-yl)-5-(trifluoromethyl)benzamide **92** (70.9 mg, 0.225 mmol, 75% yield) was obtained as a yellow oil. **Rf**: 0.35 (Pentane:EtOAc 2:1). **IR** ν 3185 (w), 3058 (w), 2931 (m), 2852 (w), 1656 (s), 1543 (w), 1482 (m), 1466 (m), 1374 (w), 1330 (w), 1256 (w), 1163 (w), 1100 (m), 1041 (w), 943 (m), 824 (w). **¹H NMR** (400 MHz, CDCl₃) δ 7.81 (br s, 1H, *NH*OCH₃), 7.64 (dd, *J* = 8.0, 1.3 Hz, 1H, *ArH*), 7.60 (d, *J* = 7.7 Hz, 1H, *ArH*), 7.45 – 7.37 (m, 2H, *ArH*), 7.35 (d, *J* = 7.9 Hz, 1H, *ArH*), 7.29 (m, 1H, *ArH*), 7.19 (s, 1H, *NCHC*), 7.15 (t, *J* = 7.5 Hz, 1H, *ArH*), 3.87 (s, 3H, *NCH*₃), 3.15 (s, 3H, *NH*OCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 166.9, 137.0, 133.6, 132.7, 132.0, 131.1, 130.9, 129.5, 128.2, 126.6, 122.7, 120.6, 119.3, 112.3, 109.8, 64.0, 33.1. **HR-ESI-MS** 337.0720 ([*M*+Na]⁺, C₁₇H₁₅ClN₂NaO₂⁺ calc. for 337.0714).

N-Methoxy-6-(1-methyl-1*H*-indol-3-yl)benzo[d][1,3]dioxole-5-carboxamide (**93**)



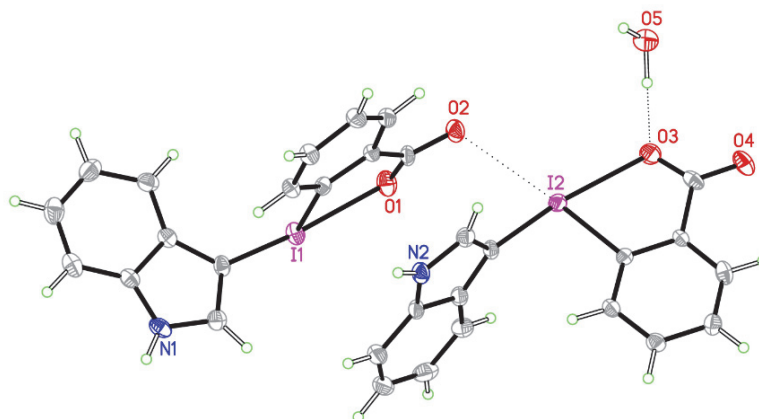
Starting from N-methoxybenzo[d][1,3]dioxole-5-carboxamide **137** (58.6 mg, 0.300 mmol), N-methoxy-6-(1-methyl-1*H*-indol-3-yl)benzo[d][1,3]dioxole-5-carboxamide **93** (78.0 mg, 0.240 mmol, 80% yield) was obtained as a white oil. **Rf**: 0.48 (Pentane:EtOAc 2:1). **IR** ν 3191 (w), 2967 (w), 2934 (w), 2899 (w), 1656 (m), 1628 (m), 1480 (m), 1448 (s), 1374 (w), 1340 (m), 1250 (s), 1224 (w), 1132 (w), 1040 (s), 1017 (w), 929 (m), 833 (w). **¹H NMR** (400 MHz, CD₂Cl₂) δ 7.49 (d, J = 8.0 Hz, 1H, Ar*H*), 7.40 (d, J = 8.3 Hz, 1H, Indole*H*), 7.33 – 7.25 (m, 3H, Indole*H*), 7.14 (ddd, J = 8.0, 6.9, 1.0 Hz, 1H, Ar*H*), 6.85 (d, J = 8.1 Hz, 1H, Indole*H*), 6.01 (s, 2H, OCH₂O), 3.84 (s, 3H, NCH₃), 3.35 (s, 3H, NHCH₃). (NHOMe proton present at 8.2 ppm) **¹³C NMR** (101 MHz, CD₂Cl₂; the signals of two aromatic carbons were not resolved) δ 166.8, 149.5, 146.1, 137.0, 129.4, 127.1, 126.9, 124.1, 122.4, 120.2, 115.2, 109.8, 107.0, 106.8, 101.7, 63.6, 33.1.

N-Methoxy-2-(1-methyl-1*H*-indol-3-yl)-1-naphthamide (**94**)

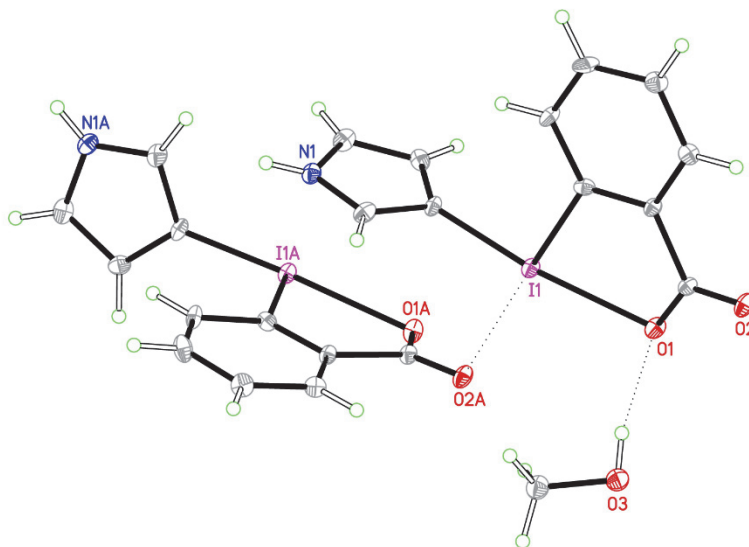


Starting from N-methoxy-1-naphthamide **138** (60.4 mg, 0.300 mmol), N-methoxy-2-(1-methyl-1*H*-indol-3-yl)-1-naphthamide **94** (78.0 mg, 0.236 mmol, 79% yield) was obtained as a colorless oil. **Rf**: 0.35 (Pentane:EtOAc 2:1). **IR** ν 3186 (w), 3056 (w), 2958 (w), 2929 (m), 2854 (w), 1651 (s), 1615 (m), 1545 (w), 1479 (m), 1384 (w), 1339 (w), 1264 (w), 1230 (w), 1134 (w), 1101 (w), 1074 (m), 1019 (m), 892 (w), 821 (s). **¹H NMR** (400 MHz, CDCl₃) δ 8.06 (d, J = 8.5 Hz, 1H, Ar*H*), 8.00 – 7.95 (m, 2H, Ar*H* + NHCH₃), 7.89 (m, 1H, Ar*H*), 7.80 (t, J = 8.6 Hz, 2H, Ar*H*), 7.58 (ddd, J = 8.4, 6.8, 1.4 Hz, 1H, Ar*H*), 7.52 (ddd, J = 8.1, 6.9, 1.3 Hz, 1H, Ar*H*), 7.41 (d, J = 9.7 Hz, 2H, Ar*H*), 7.32 (m, 1H, Ar*H*), 7.22 (m, 1H, Ar*H*), 3.86 (s, 3H, NCH₃), 3.66 (s, 3H, NHCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ 168.3, 137.1, 131.8, 131.3, 131.1, 130.0, 128.9, 128.5, 128.0, 127.6, 127.4, 126.9, 126.0, 124.8, 122.3, 120.2, 119.4, 113.1, 109.8, 64.0, 33.0. **HR-ESI-MS** 353.1256 ([M+Na]⁺, C₂₁H₁₈N₂NaO₂⁺ calc. for 353.1260).

5. Crystal Structure and DSC Measurements.

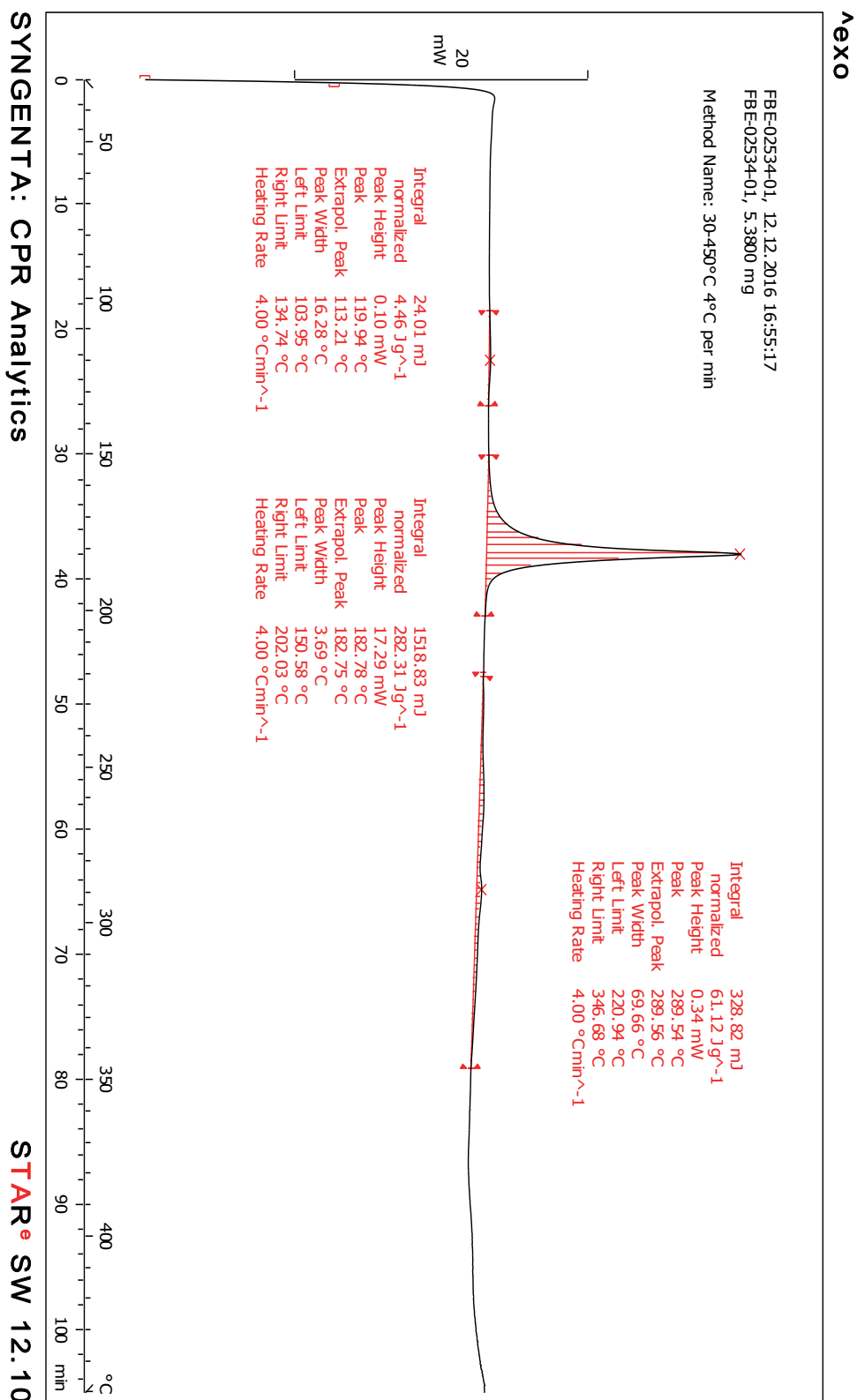


A single crystal was grown by slow diffusion of the solution of **25** in MeOD/CCl₄ mixture. Supplementary crystallographic data for this compound have been deposited at Cambridge Crystallographic Data Centre (**1540821**) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

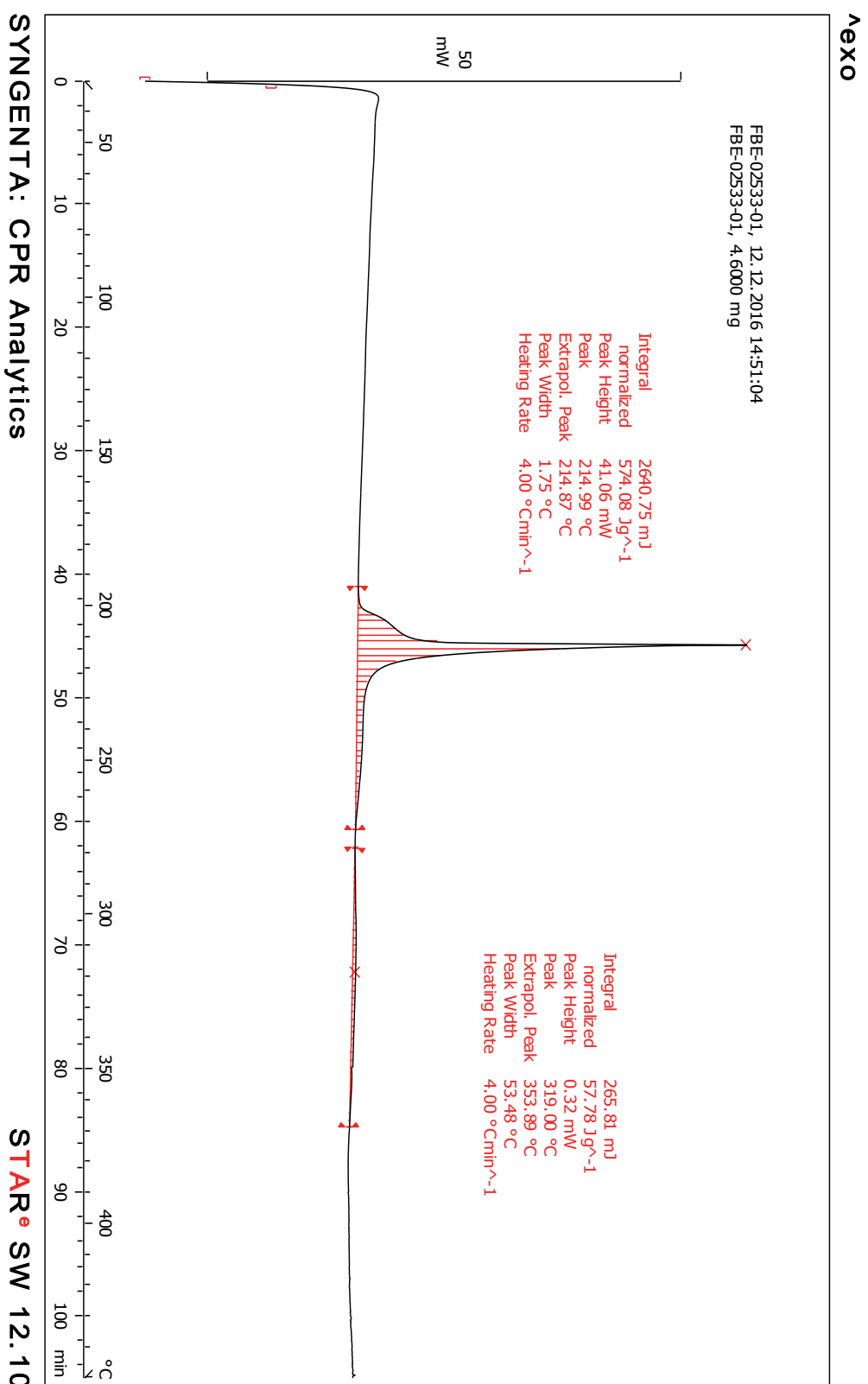


A single crystal was grown by slow diffusion of the solution of **37** in MeOD/CCl₄ mixture. Supplementary crystallographic data for this compound have been deposited at Cambridge Crystallographic Data Centre (**1541174**) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

DSC measurements of compound 21

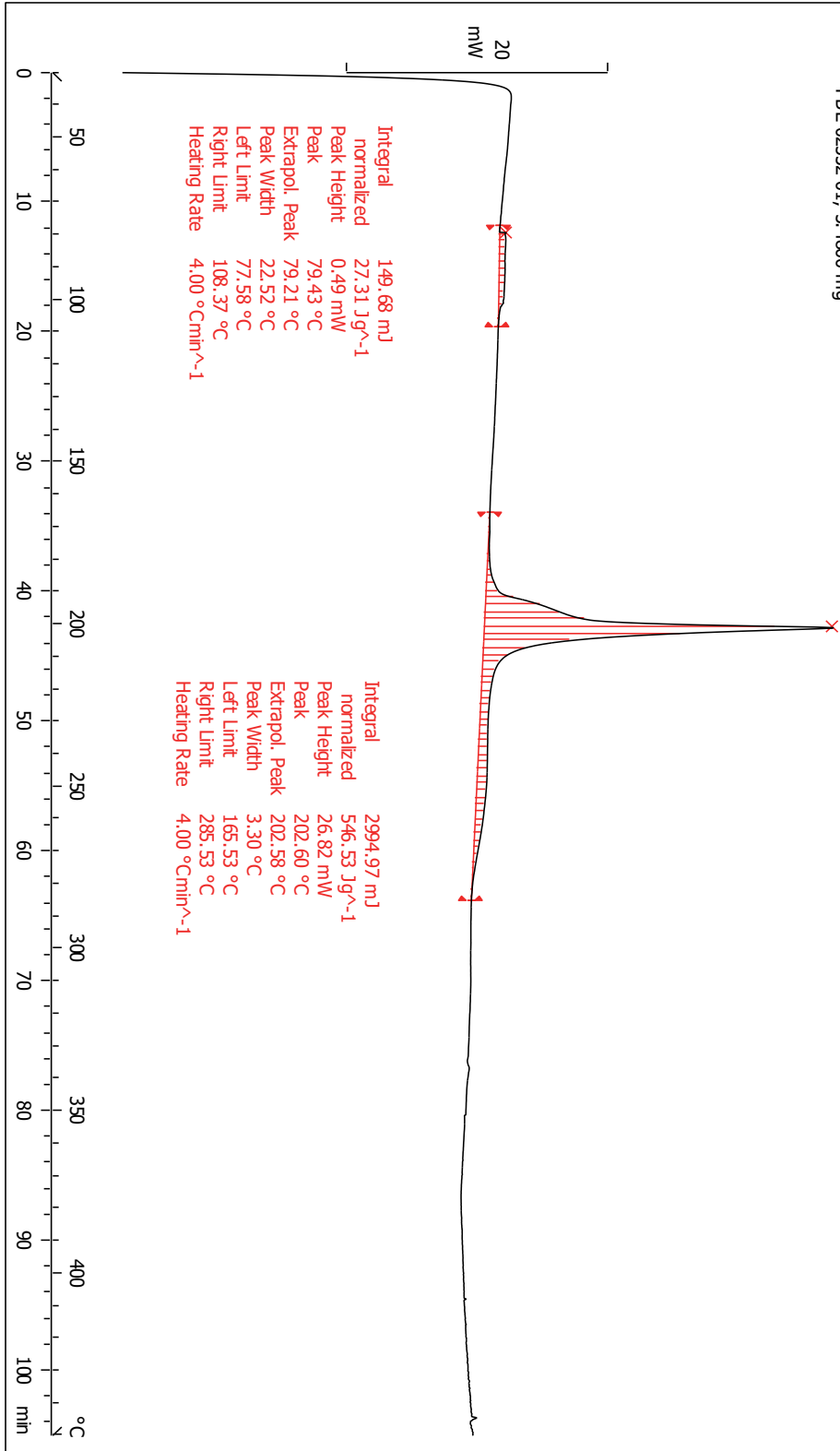


DSC measurements of compound 35a



exo

FBF-02532-01, 12.12.2016 12:46:42
FBF-02532-01, 5.4800 mg



SYNGENTA: CPR Analytics

STAR® SW 12.10

DSC measurements of compound 35b

6. Bibliography

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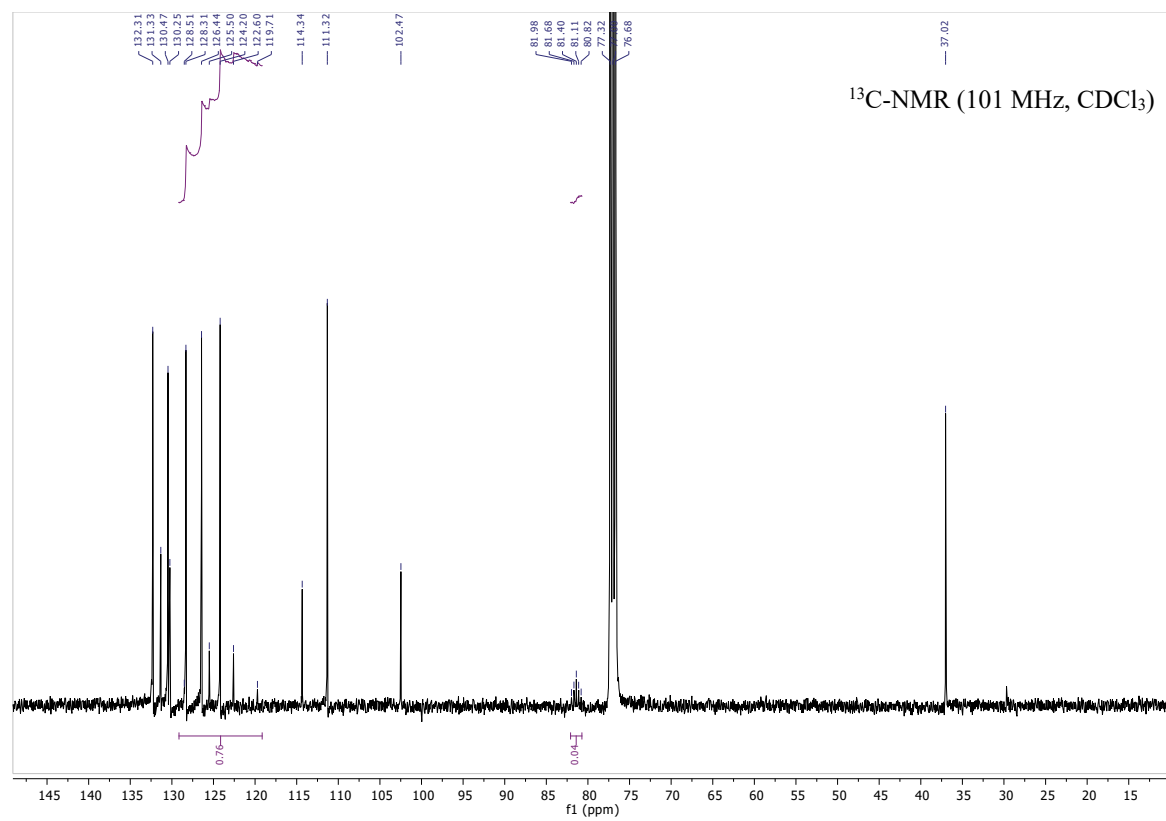
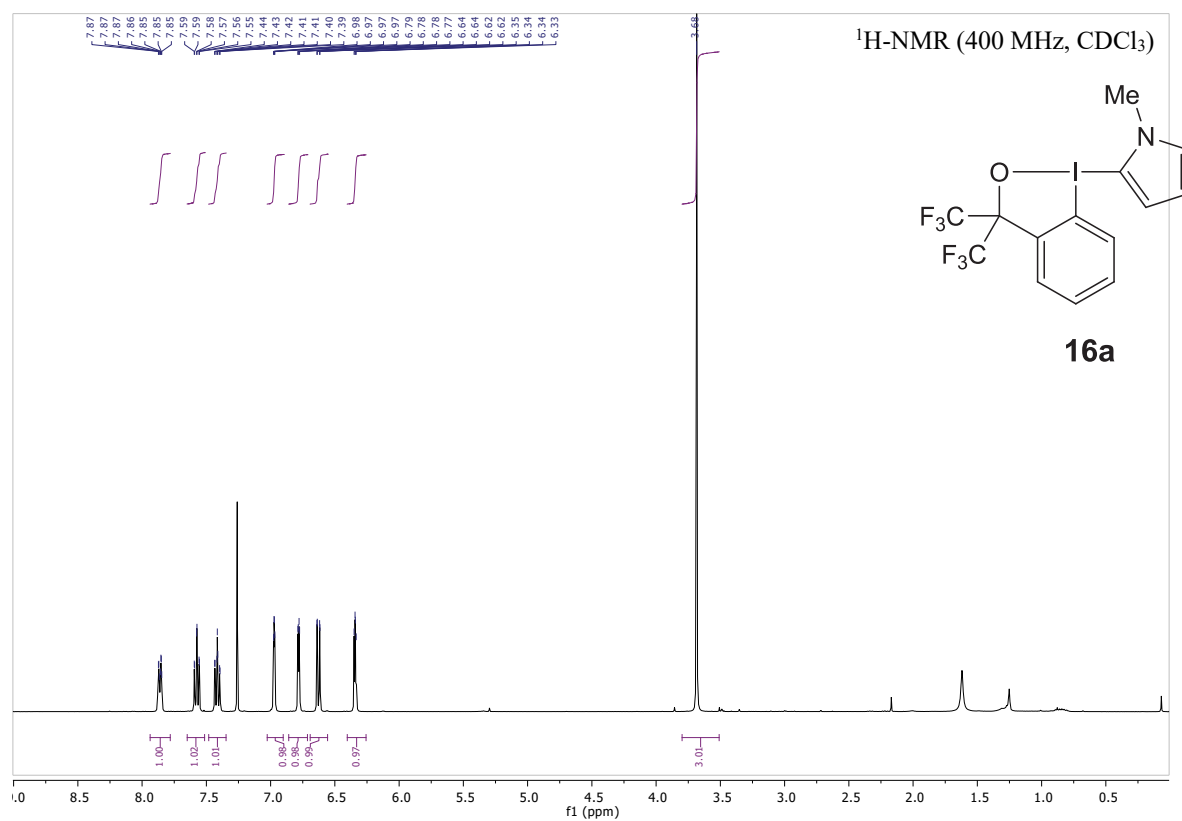
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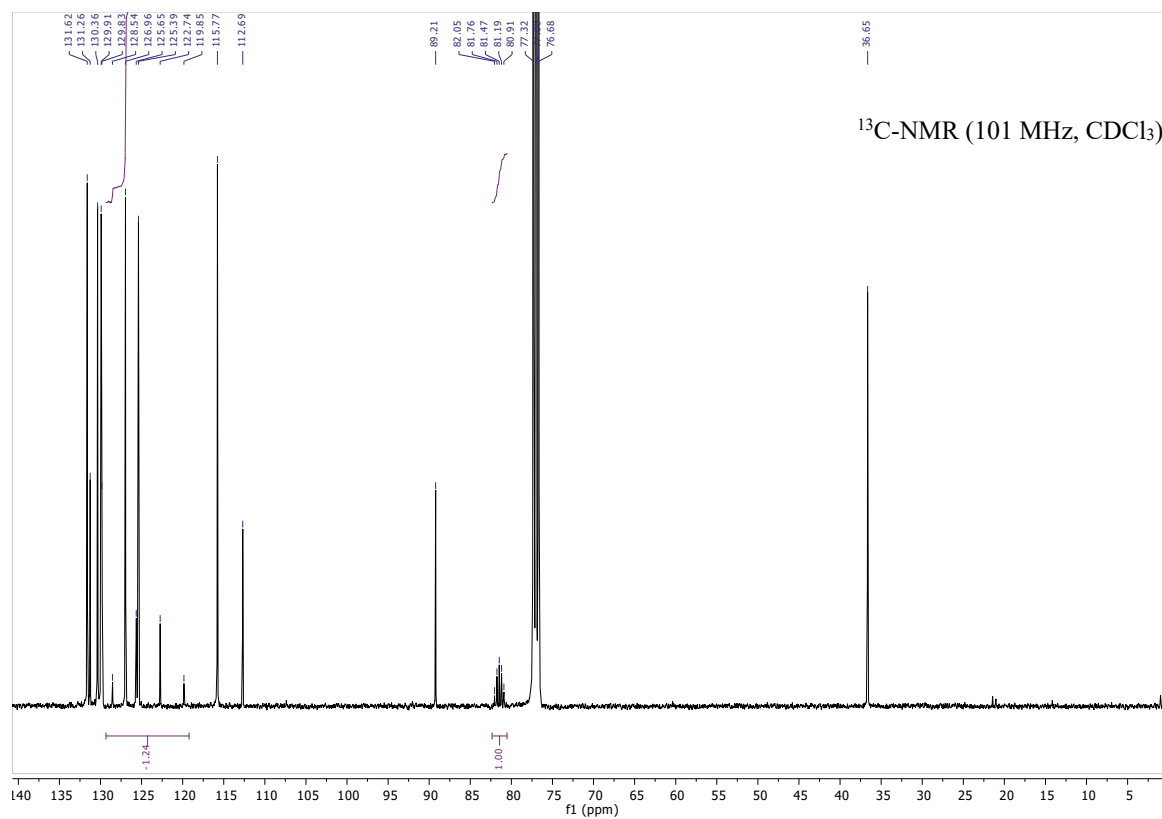
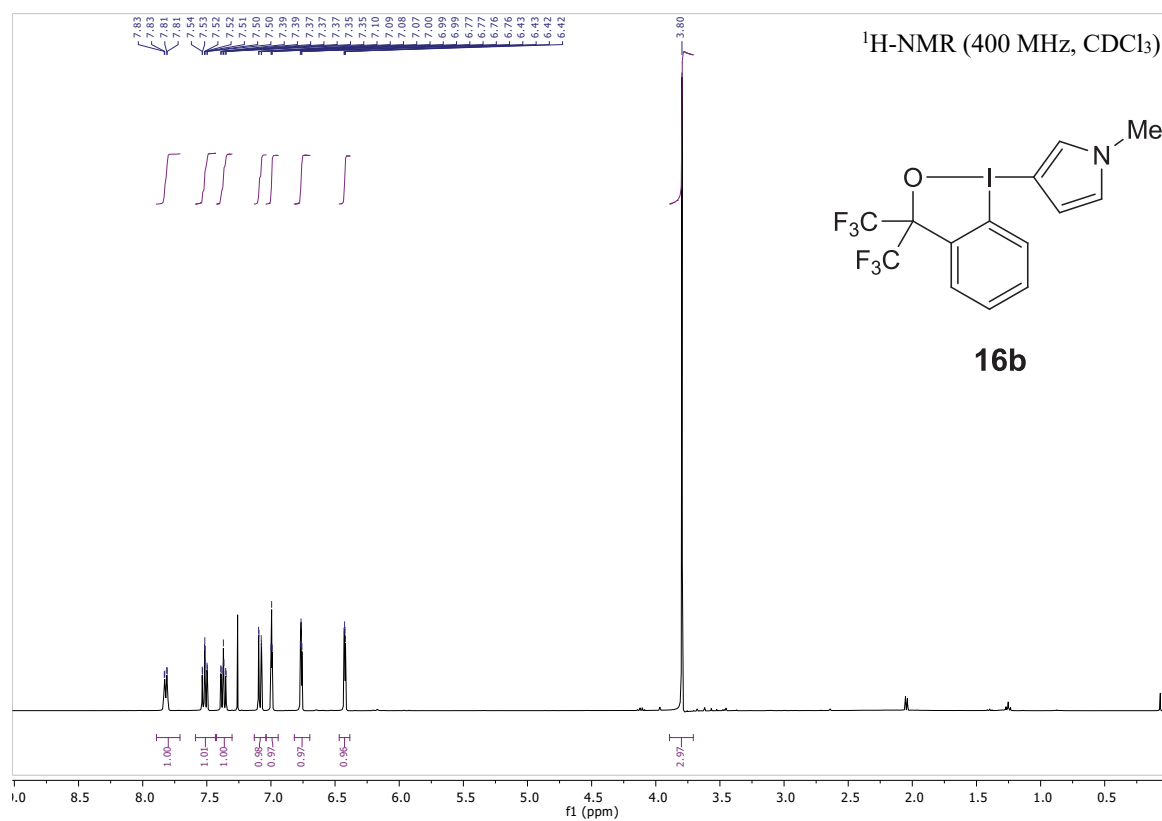
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7. Spectra of new compounds

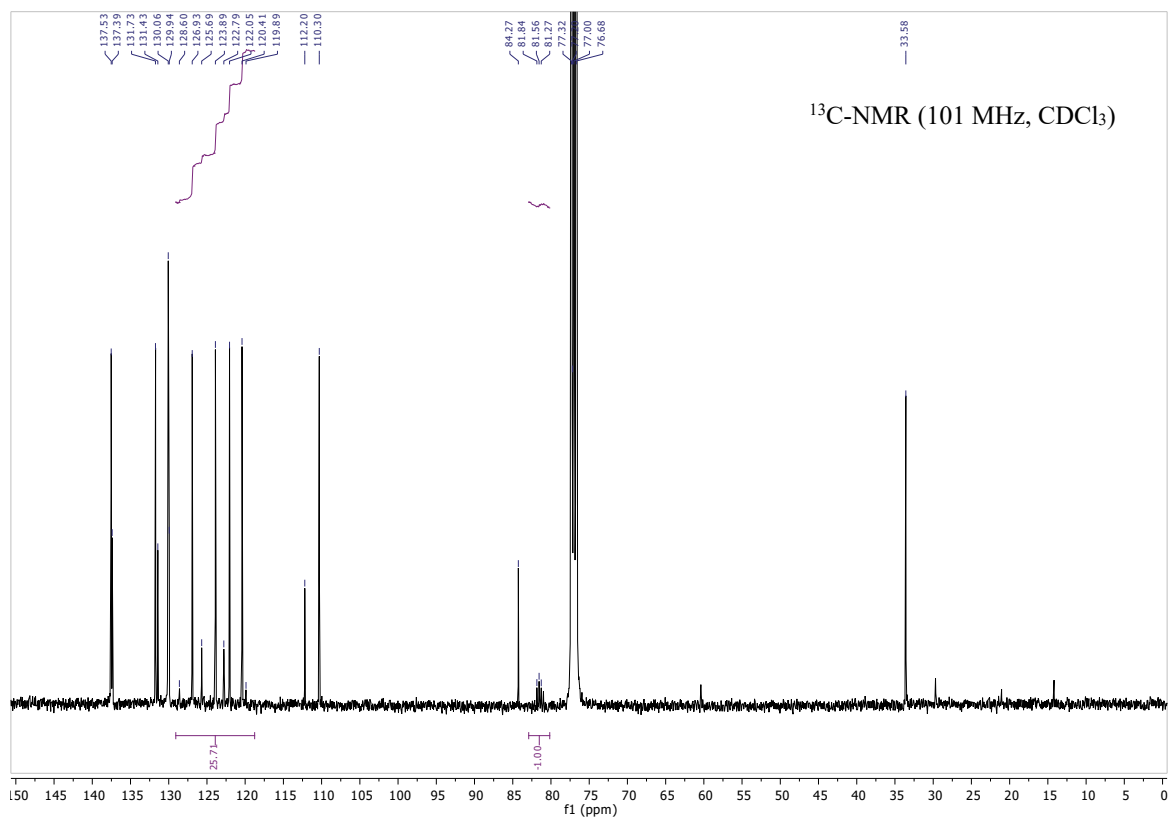
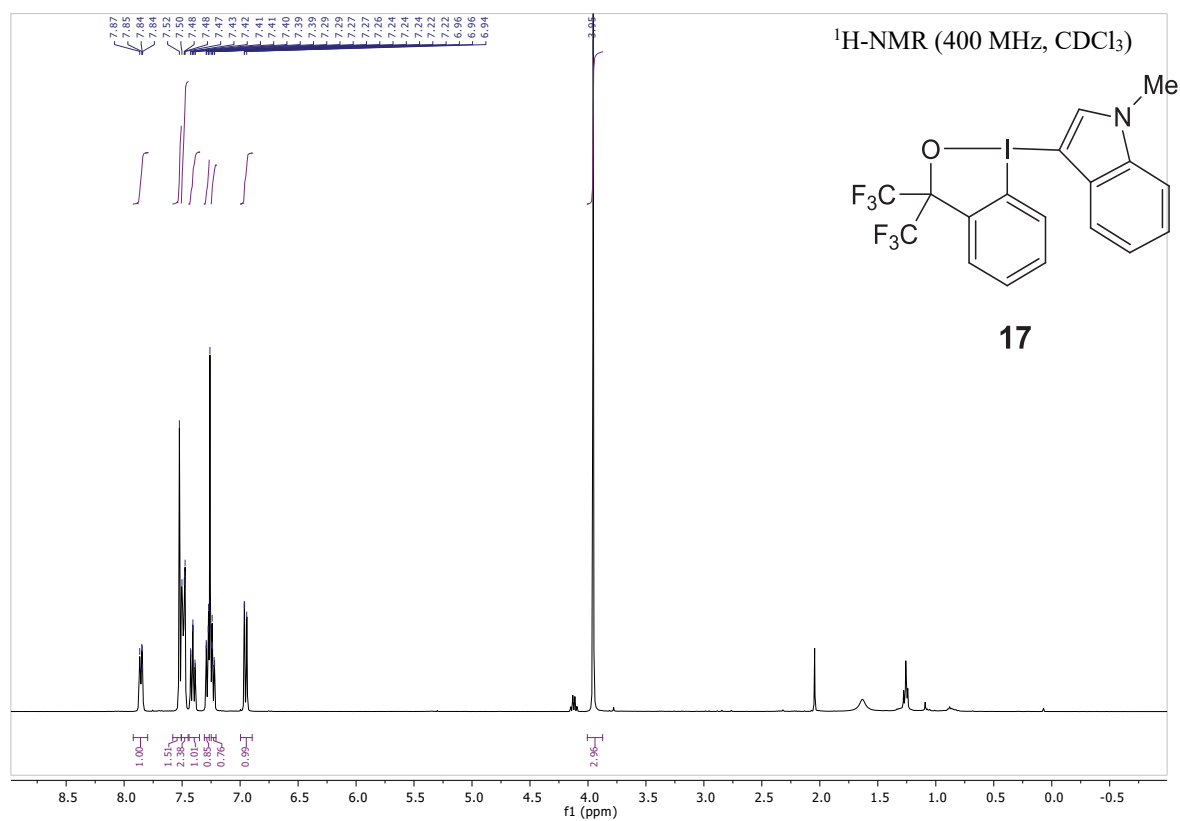
1-(2-1-Methyl-1*H*-pyrrole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1*λ*³-benzo[*d*][1,2]iodaoxole (16a)

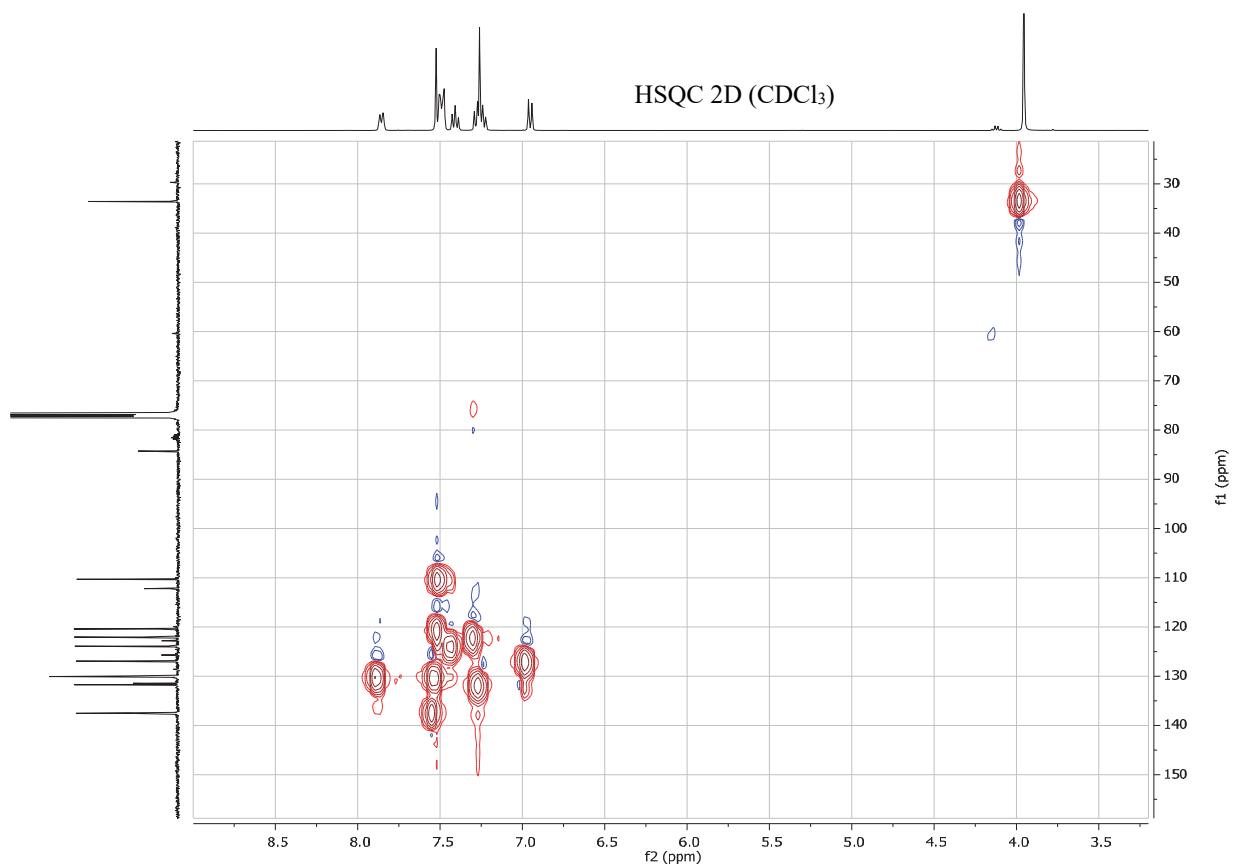
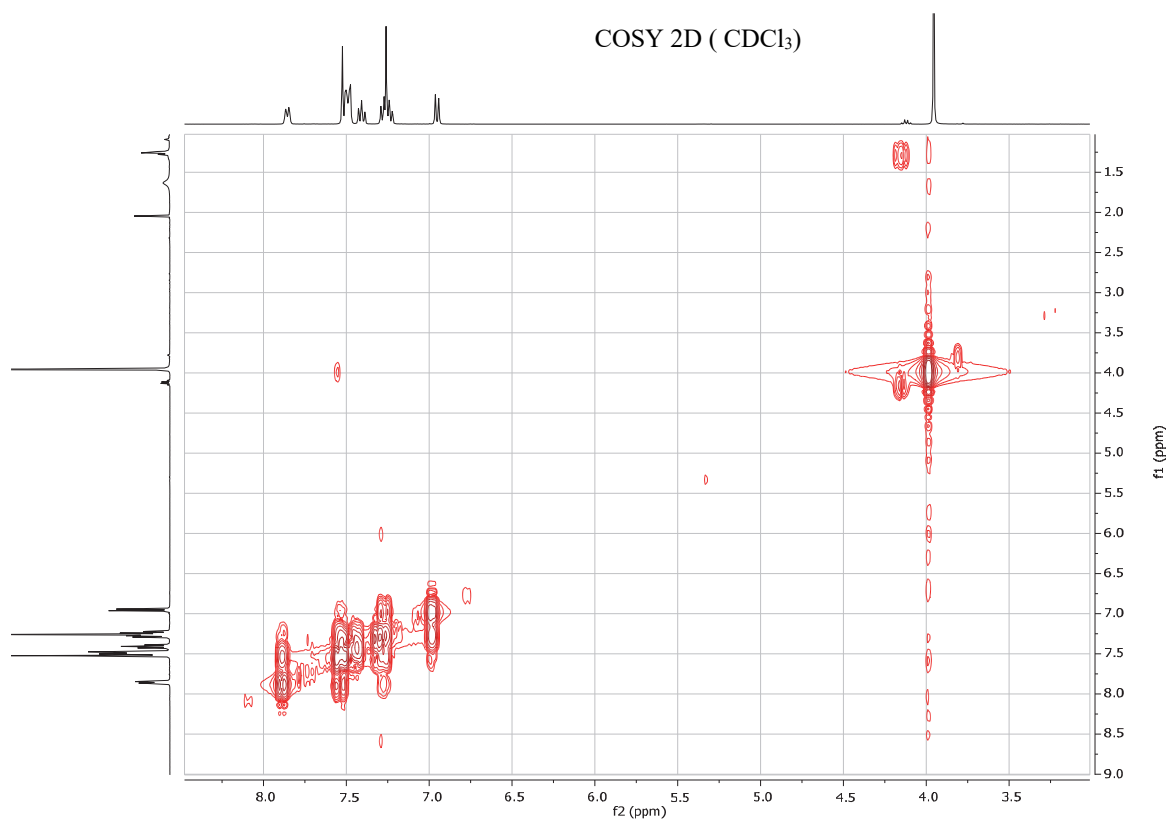


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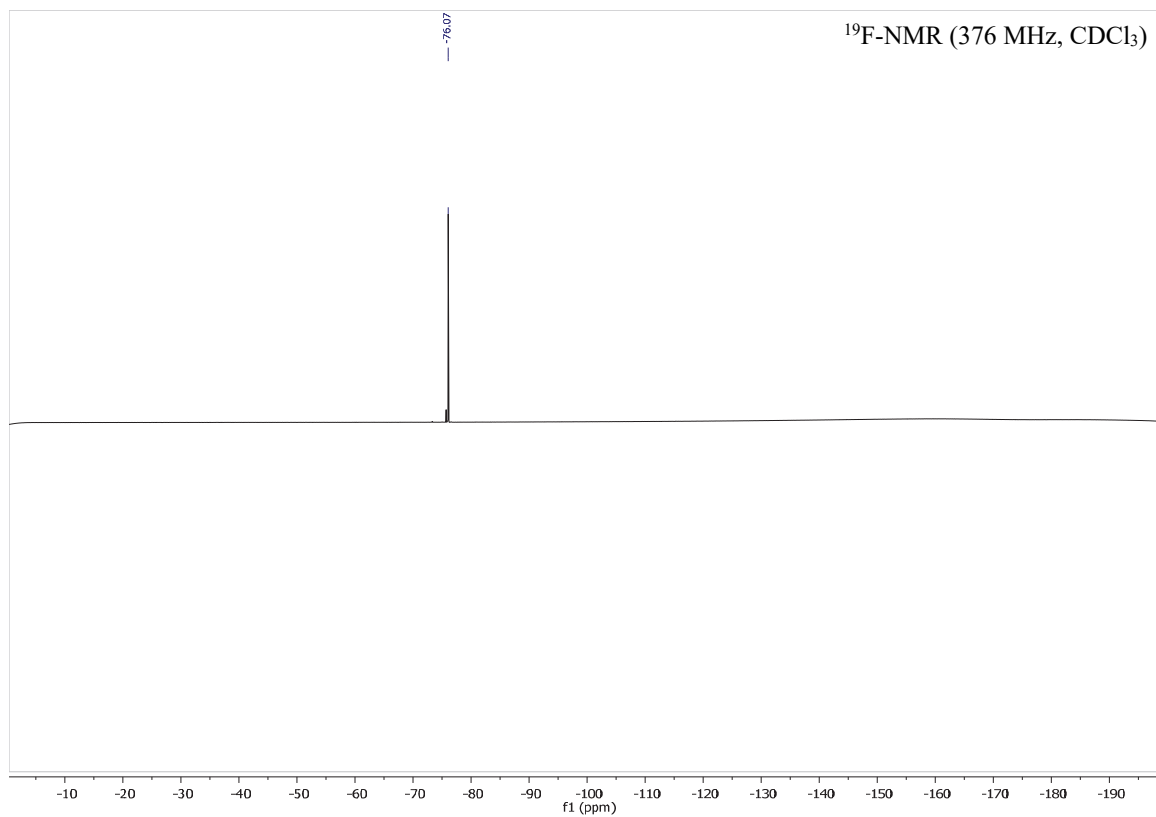
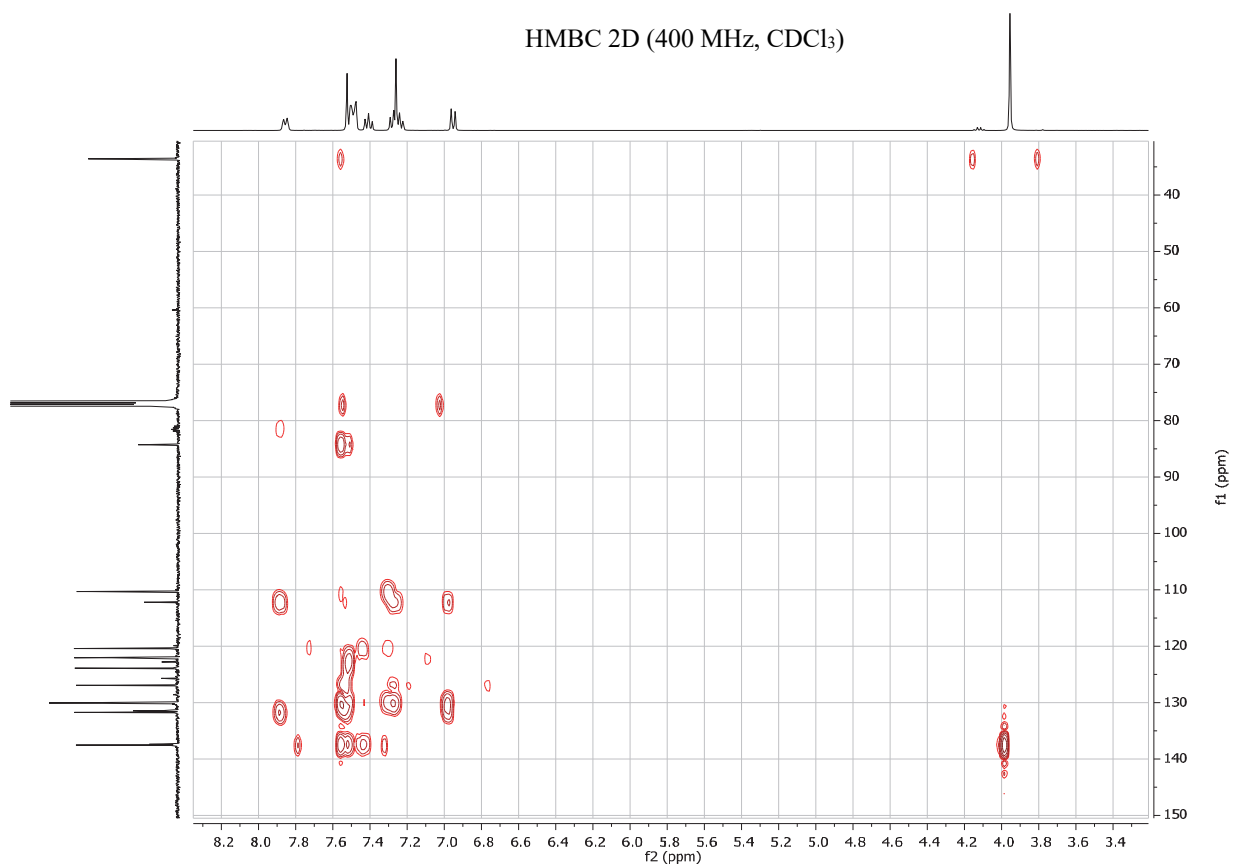


1-(3-1-Methyl-1*H*-indole)-3,3-bis(trifluoromethyl)-1,3-dihydro-1*λ*₃-benzo[*d*][1,2]iodaoxole (17)

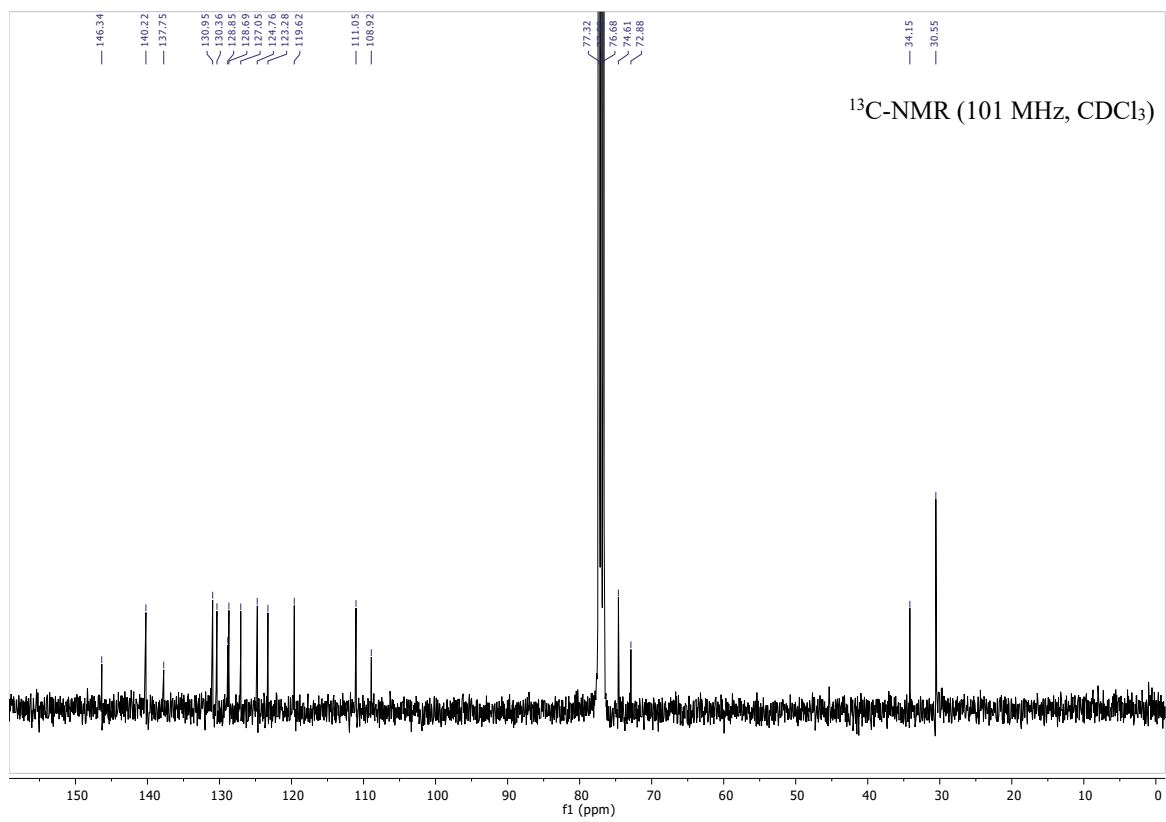
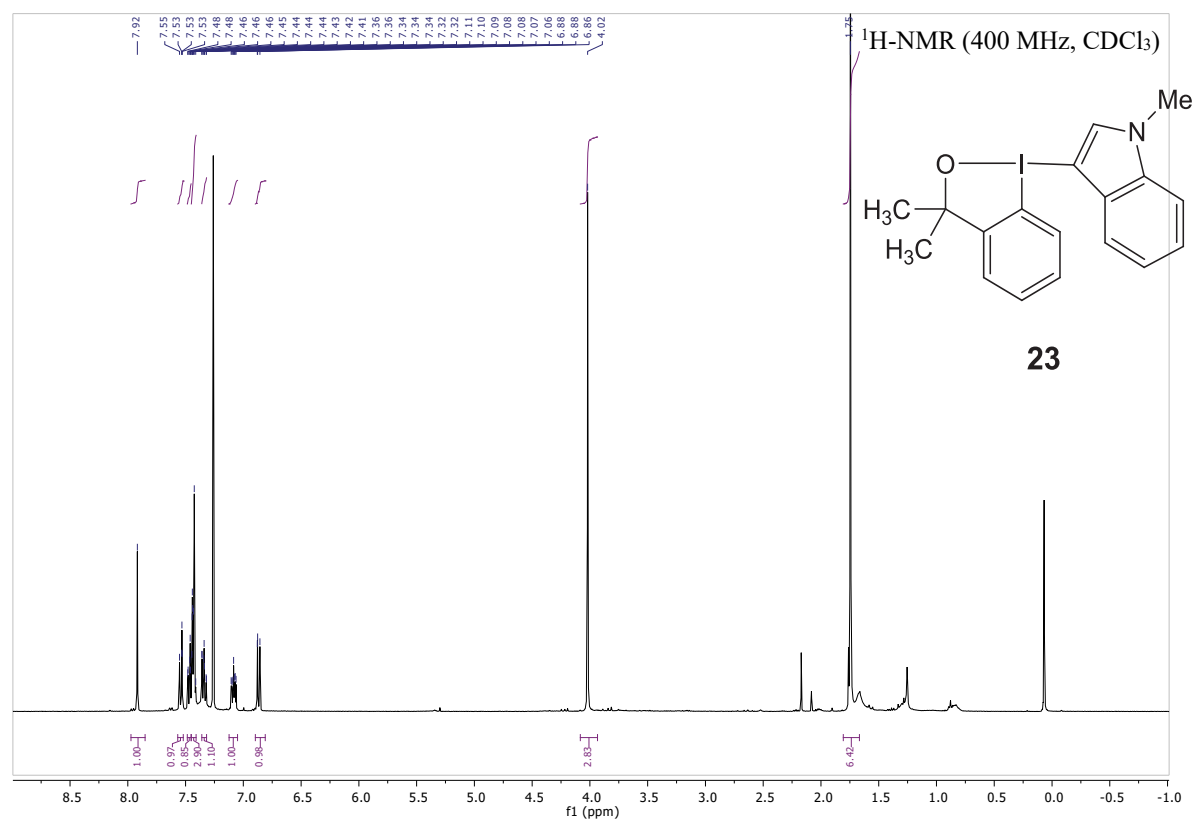




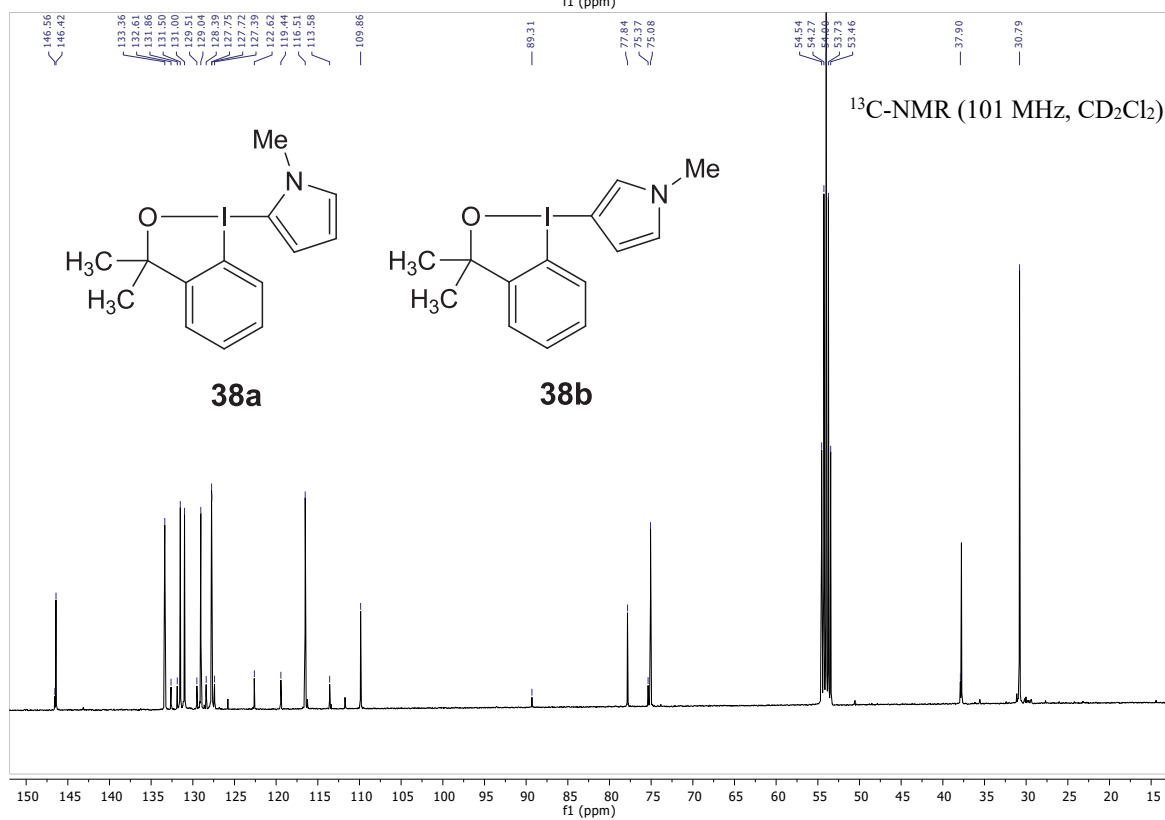
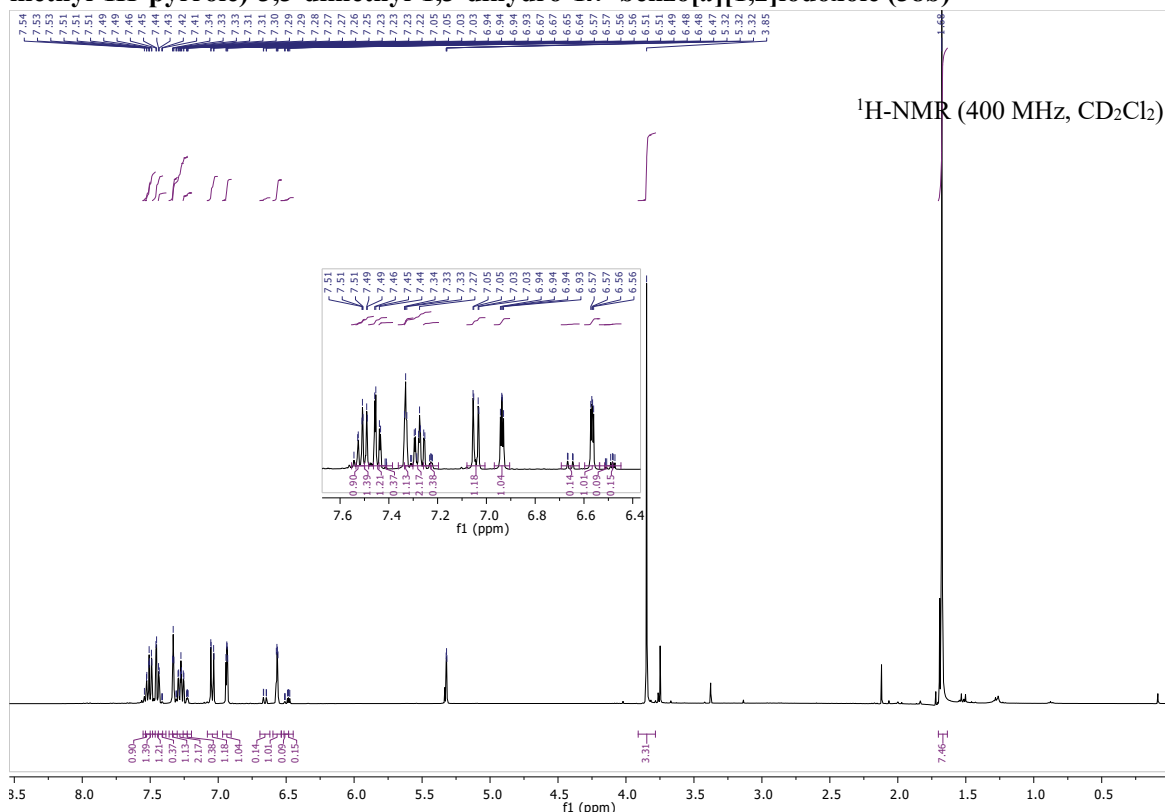
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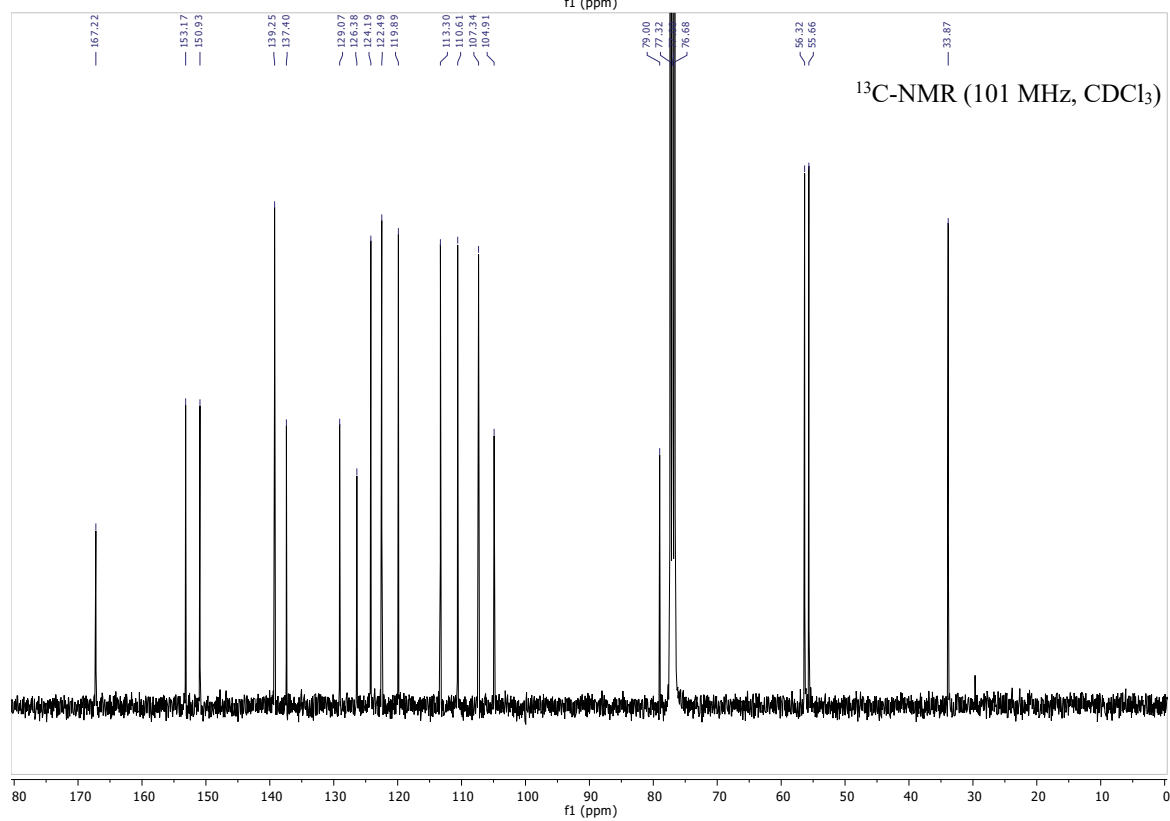
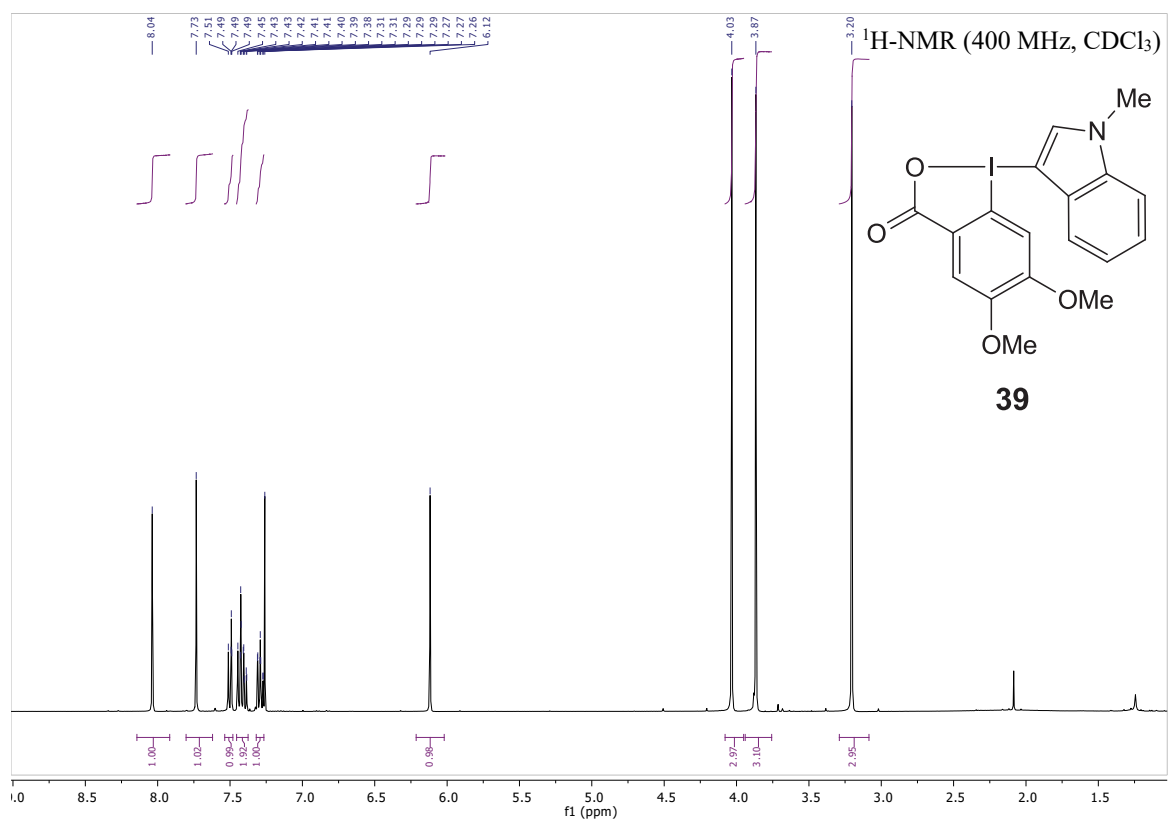
1-(3-(1-Methyl-1*H*-indole)-3,3-dimethyl-1,3-dihydro-1*λ*³-benzo[*d*][1,2]iodoxole (23)



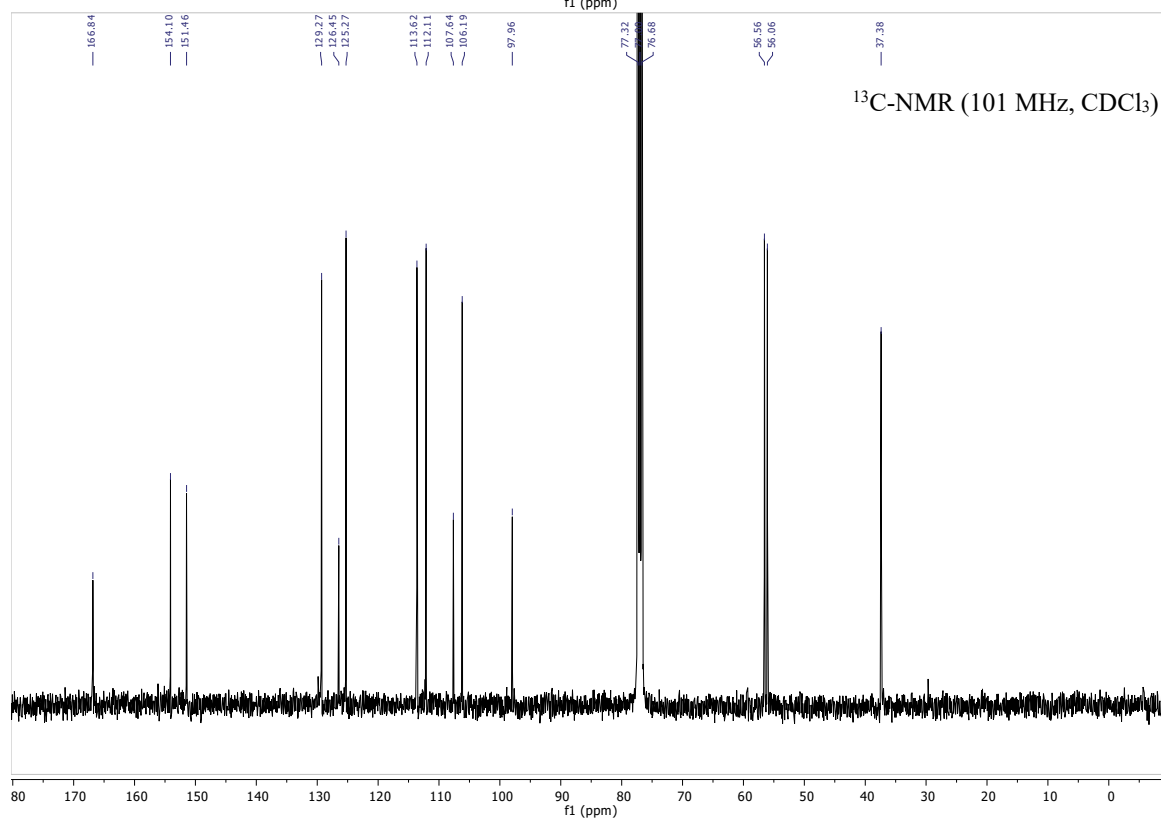
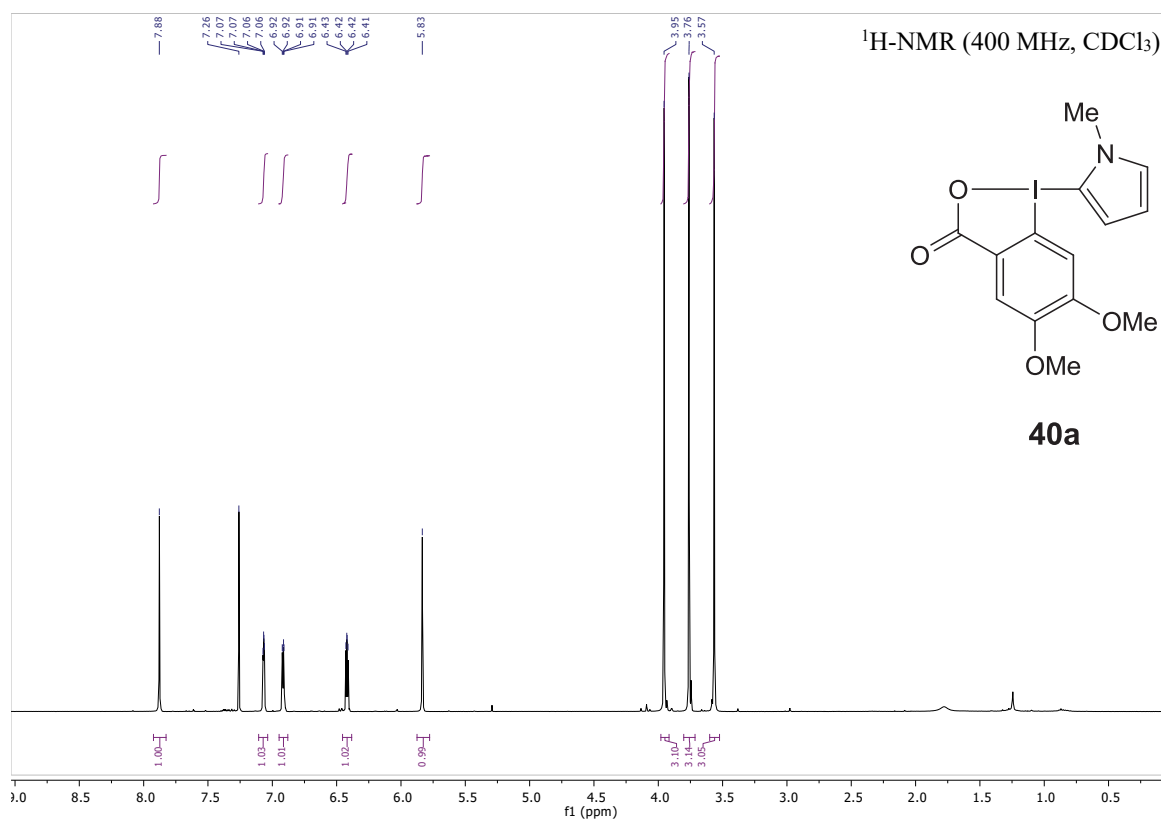
1-(2-1-Methyl-1*H*-pyrrole)-3,3-dimethyl-1,3-dihydro-1 λ^3 -benzo[*d*][1,2]iodoxole (38a) and 1-(3-1-methyl-1*H*-pyrrole)-3,3-dimethyl-1,3-dihydro-1 λ^3 -benzo[*d*][1,2]iodoxole (38b)



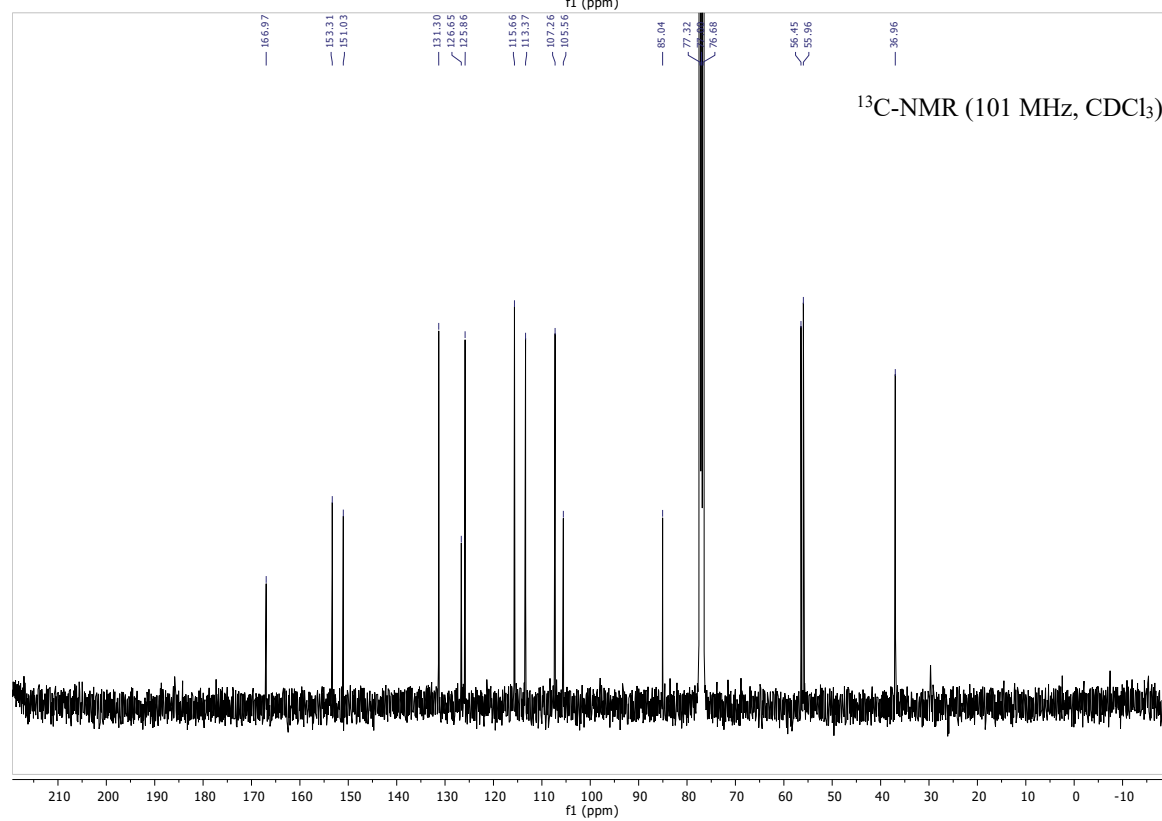
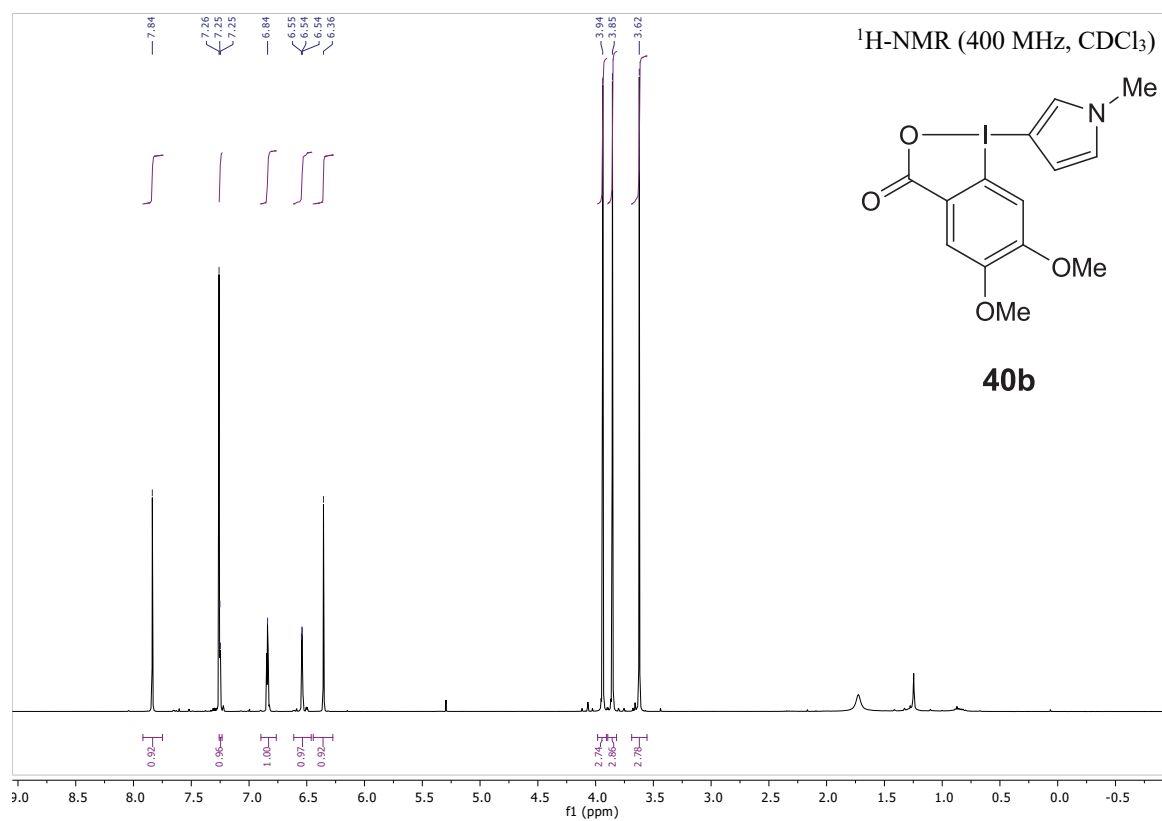
5,6-Dimethoxy-1-(3-1-Methyl-1*H*-indole)- 1*H*-1*λ*₃ -benzo[*b*]iodo-3(2*H*)-one (39)



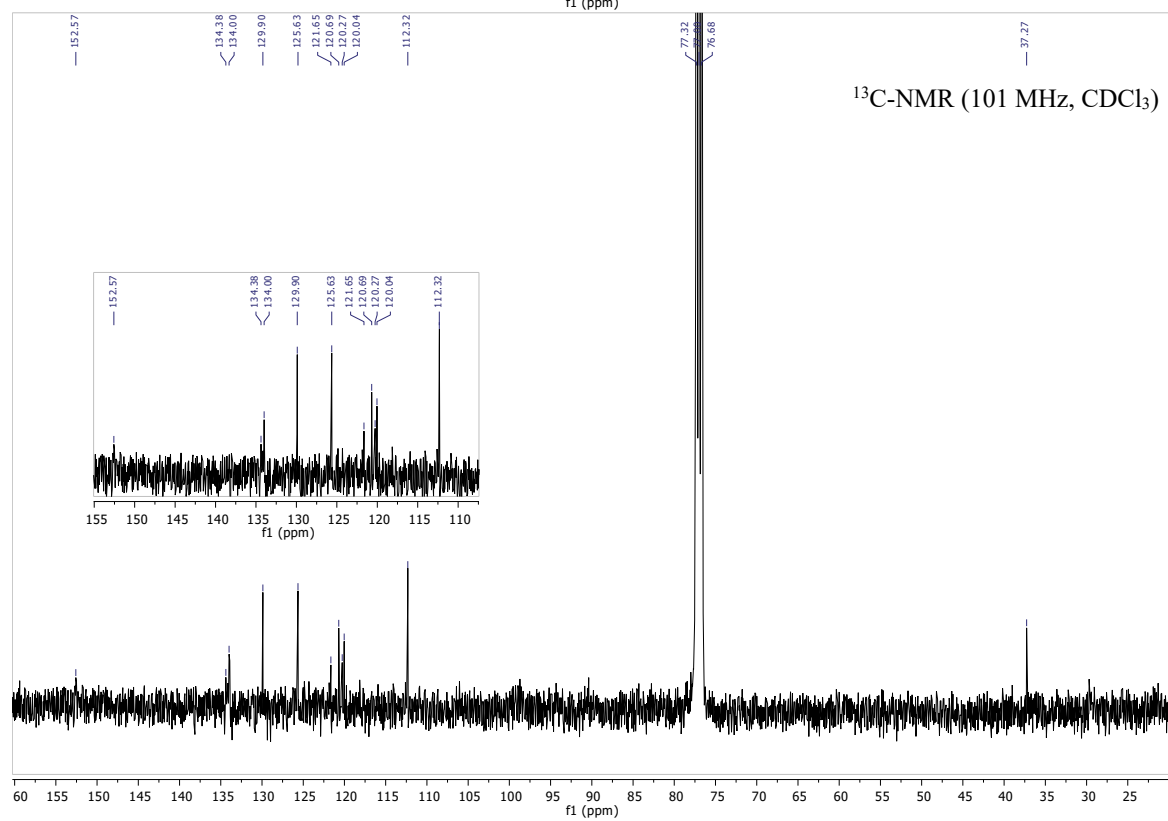
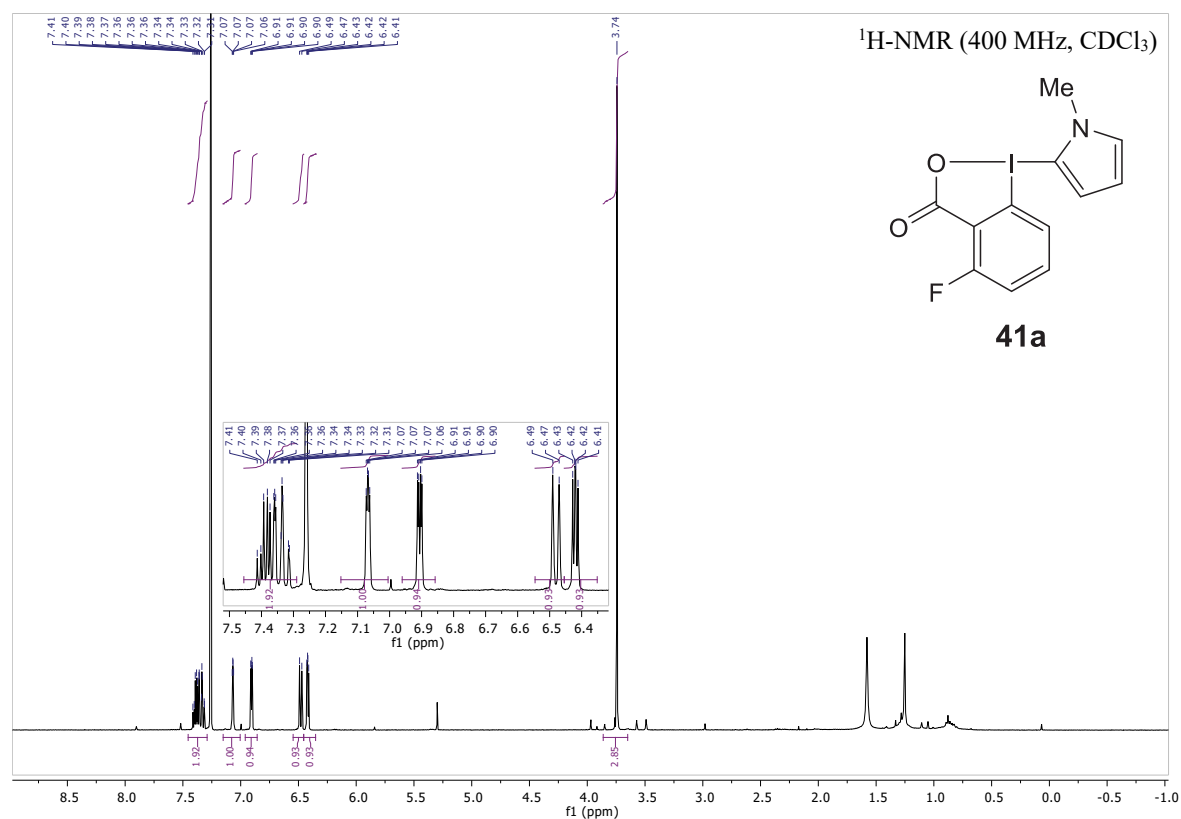
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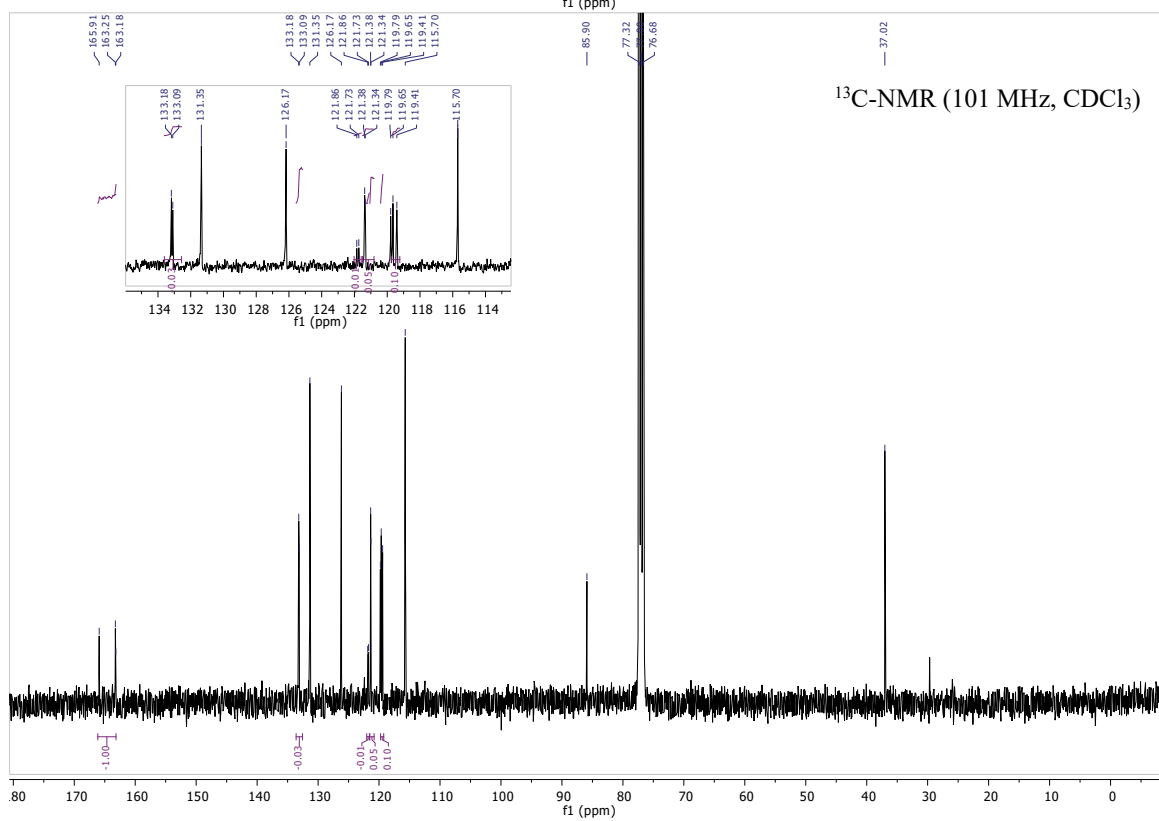
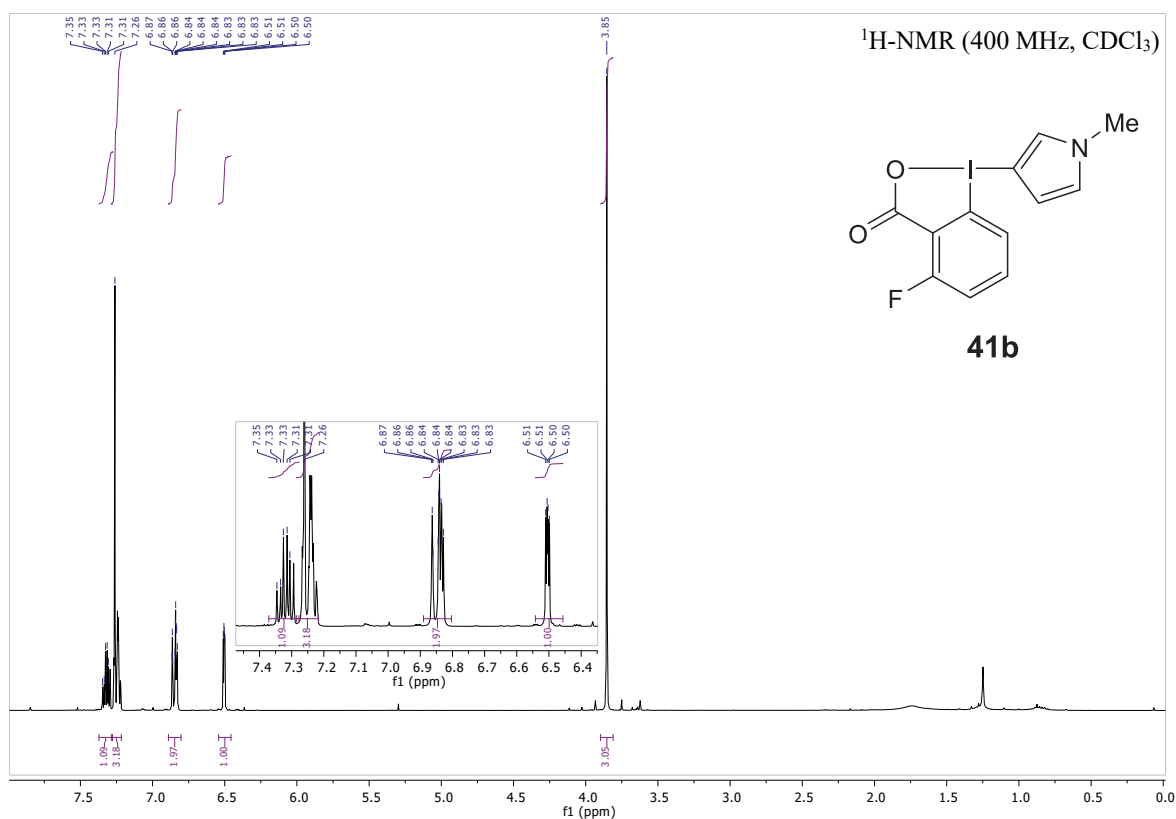
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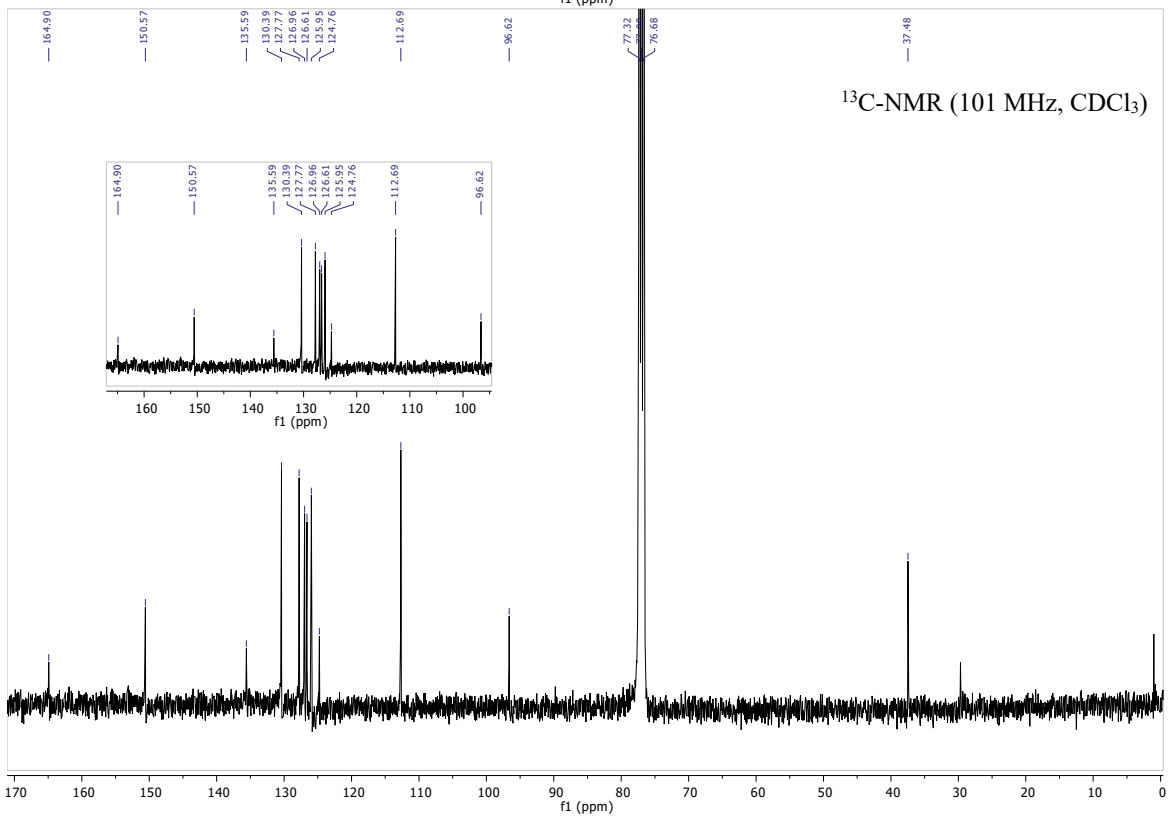
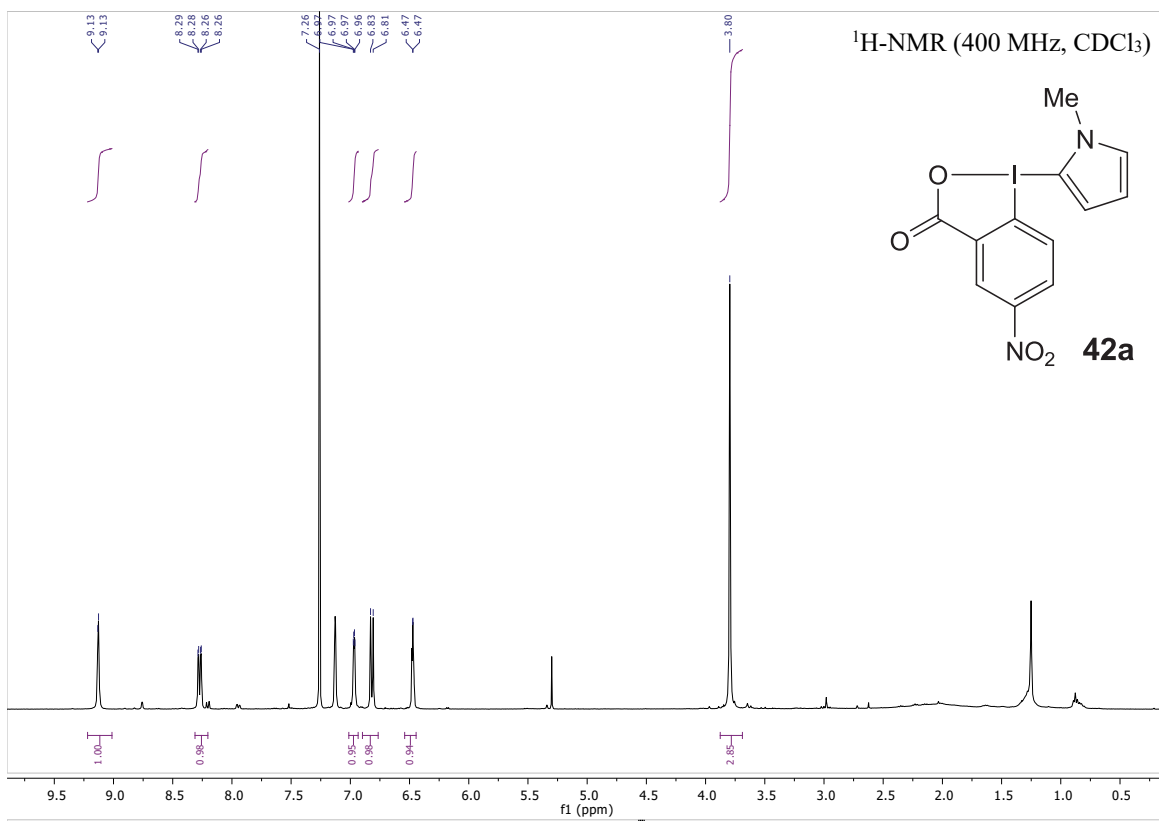
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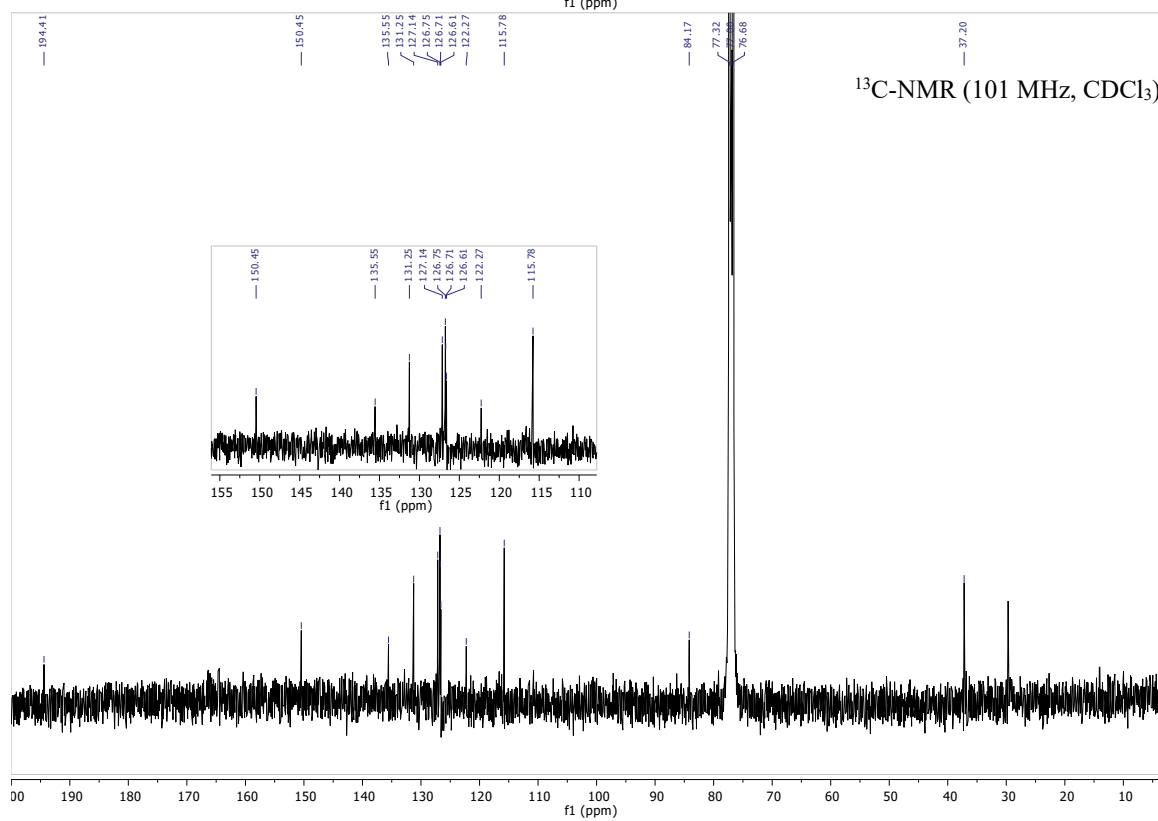
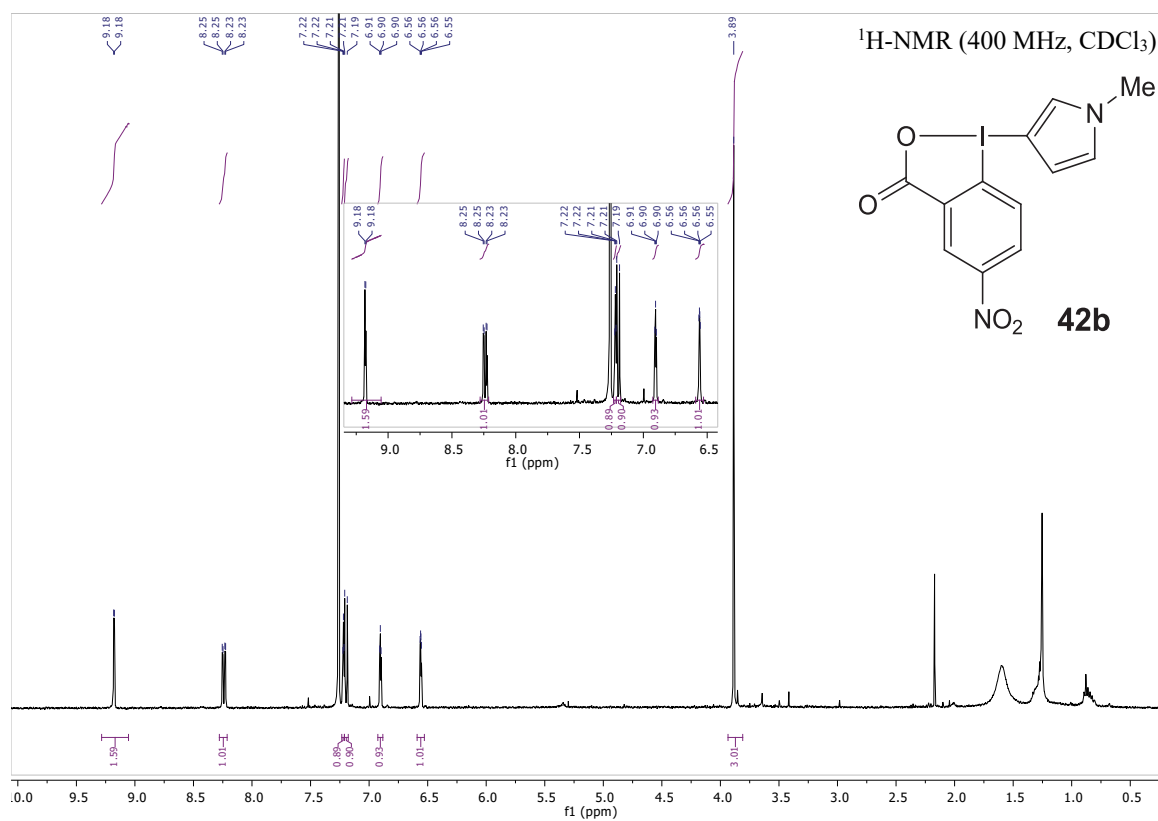
4-Fluoro-1-(3-1-methyl-1*H*-pyrrole)- 1*H*-1*λ*₃ -benzo[*b*]iodo-3(2*H*)-one (41b)



5-Nitro-1-(2-1-Methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[*d*][1,2]iodoxol-3-one (42a)



5-Nitro-1-(3-1-methyl-1*H*-pyrrole)-1*H*-1λ₃-benzo[d][1,2]iodoxol-3-one (42b)



1-(2-*D*-1-methylindole)-1*H*-1λ₃-benzo[*b*]iodo-3(2*H*)-one (49)

